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Original Communications

CLINICAL OBSERVATIONS UPON SYNCOPE AND SUDDEN DEATH IN RELATION TO AORTIC STENOSIS*

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ALTHOUGH sudden and unexpected death is regarded by many laymen as the usual conclusion of all forms of heart disease, it is actually of such infrequent occurrence as to be the distinct exception, rather than the rule. There are but few cardiac conditions which terminate with dramatic abruptness sufficiently often to make one aware of such a probability. It is widely recognized that thrombotic closure of a coronary artery is not infrequently followed by sudden death, sometimes when the patient appears to be convalescing satisfactorily, and the occasional almost instantaneous deaths of patients suffering from anginal heart failure are too well known to require comment. It has long been a matter of medical knowledge that a small proportion of patients with complete A-V heart-block die with extreme suddenness, and this type of death is thought by many to occur frequently as a result of syphilitic aortitis with aortic insufficiency. In these four distinct manifestations of cardiac disease the prognosis is properly regarded as ominous, and most physicians are aware that a patient exhibiting any one of them may die suddenly at any time.

Apparently it is not widely recognized that there is another group of cardiac patients in whom the same hazard exists, namely, that composed of patients who have stenosis of the aortic orifice. A perusal of current textbooks upon diseases of the heart reveals a singular silence in this connection; in one of them[1] there is found the suggestive comment: "Sudden death (in cases of aortic stenosis) is not very uncommon"; and Cabot[2] in his admirable study of post-mortem records emphasizes the fact that in six of the twenty-eight cases of aortic stenosis "death was

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notably sudden and unexpected, though no explanation was found for this postmortem. In one case the patient died in the hospital corridor. As a rule the death was preceded by the usual symptoms of passive congestion and stasis."

The occurrence, in the practice of one of us, of sudden unexpected death in two cases of aortic stenosis within one week led us to a systematic search of the medical literature of the past century in an effort to learn something of the apparent frequency of this association. We have found a number of casual comments upon the possibility of sudden death, or unsupported statements to the effect that death may occur suddenly, but apparently there has been no survey of this particular aspect of cardiovascular disease. A small number of case reports have been found, but the details are usually insufficient to warrant any conclusions. More than two centuries ago, Boneti[3] stated that Rayger had reported in 1672 the case of a patient who had died suddenly, and autopsy disclosed calcification of the three aortic cusps, which were "so hard that only with difficulty could a portion be cut off with a knife." In 1846, Lloyd[4] reported sudden death in a man of fifty-two years; autopsy revealed immense hypertrophy of the heart and extreme narrowing of the aortic orifice, so that a probe could scarcely be passed through it. Gautier[5] in 1860 reported that death occurred with extreme suddenness in a boy of twenty years whose heart post mortem showed aortic stenosis and normal mitral valves. In 1868, Peacock[6] reported in greater detail the case of a patient twenty-three years of age who had suffered from slight palpitation and dyspnea for seven months. Six days before death he had substernal discomfort, vomiting, and exhaustion. On the day of death his feet began to swell. Examination on that day revealed signs of aortic stenosis and insufficiency, and that evening he was found dead on the floor of the toilet, where he had fallen from the seat, and had apparently died instantly. Autopsy showed the aortic valves fused in a funnel-shaped aperture so small as to admit only the extreme tip of the little finger. The heart was two and a half times the normal weight. Budin and Decaudin[7] gave a brief report of sudden death in a woman of forty-eight who was walking around her bed in the hospital. She had presented clinical signs of aortic stenosis and insufficiency; autopsy showed aortic stenosis with thickening and fusion of the valve cusps, which were infiltrated with calcium salts.

It was not, however, until 1875 that any general connection between aortic stenosis and sudden death was mentioned. In that year, Wilks and Moxon[8] made the following interesting comment:

"In very old diseased valves, calcareous changes may take place. . . . This petrifaction is the most frequent cause of simple aortic obstruction. The earthy concretions grow into great masses that invade the valves until at last they are converted into immovable nodular masses of stone, with the orifice of the aorta reduced to a little chink of the size and shape of the mouth of the uterus. Such examples

you may sometimes meet *as causes of the sudden death of hale-looking old men who never had dropsy,* and sometimes they are found in the bodies of old men who have died of independent diseases, even when the obstruction of the aorta is nearly absolute; such cases are very surprising, and prove how comparatively innocent is simple obstruction of the orifices."

In recent years a few more instances of sudden death have been reported briefly. In 1921, Lutembacher[9] cited an instance in which autopsy revealed not only aortic stenosis of rheumatic type, but also blocking of the narrowed orifice by a large blood clot. Six years later Willius[10] reported the results of a follow-up study of ninety-six cases of aortic stenosis. Only seventy-six of these were successfully traced; of this number, fifty-six had died of cardiac disease in an average time of seventeen months after examination. In eight of these fifty-six, death had occurred suddenly. More recently Margolis, Ziellessen, and Barnes[11] studied forty-two cases of calcareous aortic valvular disease, the diagnosis being based entirely upon post-mortem examination. These authors state that sudden death occurred in five cases. "In three of these cases considerable sclerosis of the coronary arteries was found, without evidence of occlusion, however; in one case there was severe cardiac decompensation. The fifth case in which sudden death occurred was that of a woman, suffering from exophthalmic goiter associated with auricular fibrillation and congestive cardiac failure. At necropsy the coronary arteries were found not to be sclerosed but there was stenosis of the aortic valve due to fusion and calcification of the right and left anterior cusps." It is impossible to determine from their paper how great was the degree of stenosis of the valve orifice in these cases, but it was probably very slight since a clinical diagnosis of aortic stenosis was made in only two of the forty-two patients. They state specifically that occlusion of any of the larger branches of the coronary vessels was not found in any case. It is important to note that their five patients who died suddenly were in their usual health; the authors state that "a certain proportion of the patients died suddenly, although until the time of death they appeared to be *in normal health.*" Christian[12] has recently reported twenty-one cases of aortic stenosis of the calcareous type, but there was no instance of sudden death in his series. Four of the patients reported by Campbell and Shackle[13] died "absolutely suddenly without preliminary failure." It is not stated in their paper whether these four were in the atheromatous or syphilitic group, but Dr. Campbell has been kind enough to write us that three of them had atheromatous aortic stenosis, and one had syphilitic aortic insufficiency. The most comprehensive study to date is that of McGinn and White[14] who have quite recently reported upon 236 cases of aortic stenosis. Nine of the 172 deaths in this group were sudden; presumably six of these nine are those reported by Cabot,[2] since the same autopsy reports were used for both studies.

We have been able to find only one detailed report of syncope associated with aortic stenosis, although several references to the "syncope of aortic valve disease" have been encountered. Smith[15] has placed on record the report of a man thirty-six years of age who had seven or eight fainting spells in 1926, then four years of freedom, and a return of the fainting spells in 1930. The first of these occurred only with strenuous exertion, but by July, 1930, they came if he walked one block at a slightly faster rate than usual; the last one was induced by the effort of lifting his small son. Unconsciousness lasted from one-half minute to two minutes; he was pale, and cyanosis had not been noted; convulsive movements and twitching had never been observed. This patient exhibited the typical signs of aortic stenosis. The author states that "in cases of aortic stenosis with syncopal attacks, the same condition, that of cerebral anemia, probably exists, due to two principal factors: (1) the high degree of narrowing of the aortic orifice, and (2) fatigue of the left ventricle. Under conditions of stress, cerebral anemia results from the inability of the left ventricle to force blood through the narrowed orifice in sufficient amounts for the brain to function efficiently." Campbell and Shackle[16] report that syncopal attacks occurred in three of their patients with rheumatic aortic stenosis; two of them were in good health, but, in the third, anginal attacks had been followed by loss of consciousness on three or four occasions, and he died in one such attack. Four of their subjects with aortic stenosis of atheromatous or unknown origin were subject to syncopal attacks, and one of these died suddenly. The authors state that the cause of death in this last case was probably a Stokes-Adams attack, but in view of the following discussion we venture to think this improbable. Of the 236 patients with aortic stenosis reported by McGinn and White,[14] syncope occurred in 31; the authors do not discuss its cause or significance.

The infrequency of reports in the medical literature of the past eighty-five years, and the failure of practically all textbooks to mention either sudden death or syncope in connection with aortic stenosis, would lead to the impression that these occur only rarely. It is our belief that both syncope and sudden death occur with sufficient frequency to justify their association with this particular cardiac lesion, and the following report of eleven cases seems justified on the basis of its possible importance for prognosis and in order to stimulate interest in further study.

Of these patients, six were in the New Haven Hospital or Dispensary, and five were seen in private practice.

CASE REPORTS

CASE 1.—H. P. F., a white American housewife of forty-five years, had been conscious of dyspnea on exertion for several years, but had been troubled especially during the preceding six months. The effort of climbing one flight of stairs caused

considerable distress. Occasionally she awoke at night with a sense of substernal oppression and difficulty in breathing. Fatigue had been present most of the time. She had not suffered from cough, orthopnea, or edema.

She had had scarlet fever at the age of six years, and rheumatic fever at twelve years, with involvement of practically all joints. One year previously she had had severe tonsillitis, followed by another bout of rheumatic fever with multiple joint involvement. Tonsillectomy was performed shortly afterward.

Physical examination: She looked perfectly healthy. There was no cyanosis or dyspnea while at rest, and she was able to lie on one pillow without discomfort. There was no engorgement of the cervical veins. The apex impulse of the heart was visible and palpable in the fifth left intercostal space, 10 cm. from the median line. There was a short presystolic thrill at the apex and a coarse systolic thrill over the aortic area. The cardiac rhythm was regular, the rate normal. At the apex the first heart sound was moderately accentuated; it was preceded by a rumbling diastolic murmur and followed by a blowing systolic murmur. In the aortic area there was a very harsh, rough systolic murmur, well heard over the carotid and subclavian arteries; a prolonged diastolic murmur was audible beneath the upper sternum. The lungs were clear. The liver was not enlarged and there was no edema.

Electrocardiogram showed intraventricular heart-block. The blood Wassermann reaction was negative.

The diagnosis was thought to be rheumatic heart disease with stenosis and insufficiency of the mitral and aortic valves, and intraventricular heart-block.

For the next three years her cardiac condition remained practically unchanged. She continued to suffer from moderate limitation of physical exertion; one year later she thought this limitation was greater than before. The small remaining portions of tonsillar tissue were removed because of frequent sore throats and slight rheumatic pains. So far as can be learned, her last visit to a physician was six months prior to her death, when she was suffering from an acute infection of the upper respiratory tract. During the three years that elapsed between her first visit and her death, there was no apparent change in the physical signs over the heart or in the character of the murmurs. At no time did she develop signs of congestive heart failure.

One day when apparently as well as usual, she walked a short distance to visit a neighbor. On her return she paused in her own garden to pluck a flower, and fell dead.

CASE 2.—J. C. M., a white American male of thirty-seven years, had complained of excessive gas in the stomach and shortness of breath for about eight years. Ten years earlier he had been refused admission to the U. S. Army because he was said to have heart disease with mitral insufficiency; at that time he had no symptoms. About two years later he began to have slight gaseous distension after meals, and dyspnea was first noted when exertion coincided with the presence of gas. Both symptoms had become gradually but steadily worse, until they interfered greatly with his physical activity. He had never suffered from orthopnea, cough on reclining, or edema of the lower extremities. His occupation involved relatively little physical activity.

There was no history of rheumatic fever, chorea, scarlet fever, or diphtheria. Severe tonsillitis had occurred several times.

Physical examination showed a well-developed, poorly nourished man without cyanosis, dyspnea, or engorgement of the cervical veins. In the erect posture, the apex impulse of the heart was visible and palpable in the seventh left intercostal space in the anterior axillary line; with the patient recumbent, it was maximal in the sixth intercostal space just beyond the mammary line. There was a sustained systolic thrill over the aortic area, felt also in the arteries of the neck. No thrill was felt at the apex. The rhythm was fundamentally regular, but was interrupted frequently by premature beats. There was a harsh, prolonged systolic murmur and a softer

blowing diastolic murmur in the aortic area and beneath the sternum; the systolic murmur was transmitted upward, the diastolic downward. Both heart sounds were absent in the aortic area. There was a softer systolic murmur over the lower precordium, but no diastolic murmur was heard. The position of the apex impulse shifted considerably with the rotation of the patient's body, and Broadbent's sign could not be demonstrated. Blood pressure was 120-125 mm. Hg systolic, 58-64 mm. diastolic. The lungs were clear to percussion and auscultation. The liver and spleen were not palpable. There was no edema of the lower extremities or lower back.

Electrocardiogram showed frequent auricular and junctional premature beats.

A seven-foot roentgenogram of the heart showed the transverse diameter of the thorax to be 29.5 cm. and that of the heart to be 16.4 cm. The enlargement of the heart was chiefly of the left ventricle. The aorta was normal in size.

The blood Wassermann reaction was negative.

The diagnosis was thought to be rheumatic heart disease with aortic stenosis and insufficiency and mitral insufficiency. There were no clear signs of mitral stenosis.

The patient was observed at regular intervals for the next eleven months. So long as he was careful about physical activity he was perfectly comfortable, and was gradually able to increase the amount of walking and light work about his store. He slept well on one pillow and did not have edema. Approximately one year after he first came under observation he went fishing, and while standing quietly on the bank of a brook, he suddenly fell to the ground and was dead when his companion reached him within a very few seconds.

CASE 3.—J. C., a white American male of forty-one years, complained chiefly of breathlessness. In November, 1929, while doing fairly heavy work, he experienced very severe pain beneath the sternum, radiating to both arms. This pain lasted at its maximal intensity for about a half hour, and then gradually subsided. He stopped work for the day, and on the following day seemed almost as well as usual; within a short time, however, he began to have typical anginal pain beneath the sternum, radiating down both arms; nitroglycerin afforded immediate relief. For a number of months the pain occurred almost exclusively at night, and often came several times. About four or five months later, he began to have paroxysmal nocturnal dyspnea, and this continued for several months, becoming gradually worse. By May, 1930, he was forced to sit in a chair all night in order to breathe. He was unable to carry on any significant physical activity, but was not confined to bed. He grew gradually worse until September, 1930, when he was admitted to a hospital. Anginal pain had then been absent for five months.

He had had severe rheumatic fever at the age of seventeen years.

Physical examination showed a large, well-developed man, propped up in bed and exhibiting marked dyspnea and orthopnea. There was moderate pallor of the skin and mucous membranes. There was no cyanosis and little or no venous engorgement in the neck. The apex impulse of the heart was considerably beyond the mammary line, almost in the anterior axillary line, in the fifth and possibly the sixth left intercostal spaces. There was a rather harsh systolic thrill in the aortic area; no thrill was felt with certainty at the apex. The cardiac rhythm was regular, the rate normal. Systolic and diastolic murmurs were audible over the entire precordium; in the aortic area the murmurs were typical of those associated with aortic stenosis and insufficiency. The aortic second sound was absent. A mitral diastolic murmur was thought to be present, but this was not certain. Blood pressure was 122/76. The lungs showed dullness and crackling râles over both bases posteriorly. The liver edge was palpable just below the right costal margin. There was slight edema of the right foot; none of the left.

A seven-foot roentgenogram of the heart showed the total transverse diameter to be 19.5 cm., and that of the thorax 31.5 cm. There was no widening of the aortic

shadow. Electrocardiograms on two occasions showed intraventricular heart-block of slight degree, the ventricular deflections being upward in Lead I and downward in Lead III.

The blood Wassermann reaction was negative.

The signs were thought to indicate rheumatic heart disease with stenosis and insufficiency of the aortic and mitral valves; anginal heart failure due to interference with the coronary circulation, probably by distortion of the orifices of the coronary arteries; congestive heart failure.

Four days later, when the nurse entered his room in the morning, he told her he felt very well and had had an excellent night's rest. She washed his face and hands and left the room for a period of about five minutes. When she returned she found him in the same position, dead. Autopsy was not permitted.

CASE 4.—J. D., a white American male forty years of age, was admitted to the New Haven Hospital because of breathlessness on exertion; this had begun about two years previously and had slowly increased in severity. About two weeks before admission, following a severe cold with cough, he became rapidly worse, and developed orthopnea and edema of the lower extremities. The symptoms increased so steadily that his physician recommended hospital care. There was no history of rheumatic fever.

Physical examination: The patient was a well-developed, fairly well-nourished white man who exhibited marked dyspnea, orthopnea, and cyanosis. There was profuse sweating and frequent slight productive cough. The apex impulse of the heart was visible and palpable in the fifth and sixth left intercostal spaces in the anterior axillary line. There was a distinct systolic thrill in the aortic area, felt best with the patient sitting. No thrill was felt at the apex. Over the aortic area there was a very harsh, coarse systolic murmur, well heard over the carotid and subclavian arteries. The aortic second sound was absent. A soft diastolic murmur was audible beneath the sternum. A systolic murmur was audible at the apex, but no presystolic or diastolic murmur could be heard in this location. The cardiac rhythm was regular, the rate 90 per minute. The blood pressure was 110/62. The lungs showed numerous crackling râles over both bases. The liver extended about 4 cm. below the right costal margin. There was marked pitting edema of the lower extremities. There was no clubbing of the fingers or toes.

A seven-foot roentgenogram of the heart revealed considerable enlargement, chiefly of the left ventricle. The electrocardiogram showed normal mechanism.

Kahn and Wassermann tests upon the blood serum were negative.

The diagnosis was thought to be rheumatic heart disease with aortic stenosis and insufficiency, and congestive heart failure.

The patient improved and was discharged three weeks after admission, in fairly good condition. He went home and rested for two weeks, then returned to work in a wire factory. He continued working for two weeks, but noticed a return of edema in the lower extremities, dyspnea, orthopnea, and cough. Because of an increase in the severity of these symptoms he was taken to a hospital, where he remained for five weeks. He was discharged, again comparatively free of symptoms. and went home for three weeks. During this period, the dyspnea and orthopnea returned, and he spent much of the time in bed. Symptoms were induced by the slightest exertion, and he would awaken several times at night with a sense of suffocation, relieved by sitting up. He was again admitted to the New Haven Hospital.

During the fifty-seven days that he remained in this hospital he was propped up in bed or in a chair constantly. Digitalis was continued in maintenance doses, and he received various diuretics at frequent intervals. Despite these measures he became slowly but steadily worse. During the last two weeks of life, his condition changed very little from day to day. One morning he was sitting quietly in bed

while the nurse washed his hands. He suddenly became intensely cyanotic, and respirations ceased within a few seconds. Death occurred in about a minute.

Autopsy was performed the same day. The weight of the heart was 900 grams; the wall of the right ventricle measured 6 to 7 mm. in thickness, that of the left 18 mm. The pulmonary and tricuspid valves appeared normal in all respects. The mitral valve leaflets were thin, flexible, and normal in appearance, except for a few small, discrete, firm, translucent nodules along the free edges. These nodules measured 2 to 3 mm. in diameter, and felt like deposits of calcium within the valves. There was no stenosis of the mitral orifice. The aortic orifice, as seen from above, appeared to be a tiny slit; it measured only 6 to 7 mm. in its greatest diameter, and was so distorted that the original boundaries of the individual valve cusps could not be determined; they remained only as greatly thickened, fused, calcified structures. On the aortic surface of the anterior cusp, there was a small friable ante-mortem thrombus. The orifices of the coronary arteries were patent, and careful dissection of all the major branches failed to reveal any occlusion. Microscopically, the only significant change consisted in enormous hypertrophy of the muscle fibers. No increase in connective tissue was seen.

CASE 5.—F. R., a Jewish woman of twenty-nine years, stated that she had suffered from dyspnea on exertion for about ten years. This symptom was said not to have increased in severity during the past two or three years. She had never had orthopnea, cough on reclining, pain over the liver, or edema. She had suffered from severe rheumatic fever in early adult life.

At the time of her first visit to the New Haven Dispensary, physical examination revealed slight cyanosis of the lips. There was no venous engorgement in the neck, and no dyspnea while at rest. The apex impulse of the heart was visible and palpable in the fifth left intercostal space in the anterior axillary line. A presystolic thrill was palpable over the apical thrust and a coarse, prolonged systolic thrill in the second right intercostal space near the sternum. The cardiac rhythm was regular and the rate normal. At the apex the first heart sound was greatly accentuated and continued into a blowing systolic murmur; the second sound was followed by a low-pitched murmur that extended through most of diastole. In the aortic area there was a loud, harsh systolic murmur transmitted to the arteries in the neck; a prolonged diastolic murmur was audible beneath the upper sternum and along the left sternal border. The position of the apex impulse shifted several centimeters with rotation of the patient's body. The blood pressure was 144/86. There were no signs of visceral congestion and no edema. The blood Wassermann reaction was negative.

The physical signs were regarded as those of rheumatic heart disease with stenosis and insufficiency of the mitral and aortic valves.

Five and a half years later she was admitted to the New Haven Hospital because of slowly increasing congestive heart failure. For some months she had suffered from dyspnea, orthopnea, and physical weakness. The heart was found to have increased greatly in size during the intervening years; the apex impulse was in the sixth left intercostal space beyond the anterior axillary line. The rhythm was totally irregular, the rate normal. The heart sounds and murmurs were as described above. The blood pressure was 140-146 mm. Hg systolic, 80-90 mm. diastolic. The liver was slightly enlarged but not tender. There was no edema.

Fluoroscopic examination confirmed the clinical finding of great cardiac enlargement, and revealed conspicuous dilatation of both auricles. Electrocardiogram showed auricular fibrillation and digitalis depression of the S-T intervals in Leads I and II; there was no axis deviation. The urine contained a faint trace of albumin, but was otherwise normal. The Kahn reaction on the blood serum was negative. Other laboratory examinations revealed nothing of significance.

She remained in the hospital for twenty-five days, most of the time at complete rest in bed. Digitalis was continued in doses sufficient to control the cardiac rate; other treatment was purely symptomatic. There was steady improvement, and she left the hospital feeling quite comfortable. About one week later she suddenly fell dead in her home. Autopsy was not performed.

CASE 6.—J. L., a Jewish man of fifty-eight years, was admitted to the New Haven Hospital because of symptoms of heart failure. He had noticed moderate breathlessness on exertion for several years, but it had not interfered seriously with his activity until several months before. Two weeks prior to his admission, he stopped work in order to rest for a week, but his improvement was not great, and on the morning of admission he found he was unable to walk even the short distance to a trolley line.

A review of his past and family histories revealed no items of importance.

Physical examination: The patient was rather emaciated. There was considerable dyspnea while at complete rest, greatly increased by slight exertion. There was slight cyanosis of the lips; no venous engorgement in the neck. The apex impulse of the heart was visible and palpable in the fifth and sixth left intercostal spaces beyond the mammary line. There was a short thrill over the apex, thought to be presystolic in time, and a coarse sustained systolic thrill over the aortic area. The cardiac rhythm was regular, the rate normal. In the aortic area there was a loud, rough systolic murmur transmitted to the arteries of the neck. The aortic second sound was absent. There was a prolonged diastolic murmur beneath the sternum. At the apex there were systolic and diastolic murmurs, different in quality from those at the base. Blood pressure was 138/70. The lungs showed dullness and numerous crackling râles over the lower portions. The liver edge was just above the level of the umbilicus. There was no edema. The Wassermann reaction on the blood serum was negative.

The physical signs were interpreted as indicating rheumatic heart disease with stenosis and insufficiency of the aortic and mitral valves, and congestive heart failure.

He was admitted to the hospital about 7 P.M. and received morphine hypodermically at once. He vomited small amounts of fluid at 10 P.M. and at 3:30 A.M. He was not regarded as critically ill; his condition was such that it was believed he would improve with rest and medication. He seemed to be quite comfortable until 4:50 A.M., when there was sudden extreme respiratory distress and he was dead within several minutes.

Autopsy: The heart weighed 750 grams. There was marked sclerosis of the coronary arteries, but no obstruction could be found in any of them. The three cusps of the aortic valve were very rigid, brittle, and fused together into a calcified mass which projected into the aorta like a crater. The orifice at its widest diameter measured 1 cm.; it was completely occluded by a blood clot which was firmly adherent to the free edges of the valve. At the point of adhesion, the thrombus was pale and friable; in the center it was dark red and elastic. The orifices of the coronary arteries were not obstructed. The cavity of the left ventricle was relatively enormous. The wall of the right ventricle was 6 mm. in thickness, that of the left was 18 mm. The mitral orifice was considerably narrowed by fusion of the valve edges. The leaflets were thickened, especially at the free edges and were less freely movable than normal. At the point of fusion of the two valves anteriorly, the endocardium was replaced by a rough calcareous area. The chordae tendineae were thickened. The pulmonary and tricuspid valves were normal in size and appearance. Microscopic examination revealed a great increase in size of the muscle fibers of the left ventricle. Scattered throughout the walls of this chamber were small collections of mononuclear leucocytes; these were located chiefly about the arterioles, but some of them were seen transecting groups of muscle fibers. Some sections of the left ventricle showed great increase in connective tissue.

It is interesting to know that six years earlier this patient had reported at the New Haven Dispensary because of pain in the left wrist, present for two days. The following note was made at that time by the interne:

"The heart shows a systolic thrill over the aortic area and a very loud systolic murmur over the greater part of the upper right chest and along the arteries of the neck; it is loudest over the aortic area. There are systolic and diastolic murmurs at the apex. Pulse is of the plateau type. Blood pressure 140/100. Impression: Aortic stenosis and insufficiency."

CASE 7.—K. J., an American housewife of forty years, was first seen in the New Haven Dispensary in February, 1923. At that time she stated that she had suddenly lost consciousness four times in the preceding two years, and on many occasions had felt faint without actually losing consciousness. She remained unconscious for from three to thirty minutes, and on one occasion she is said to have been cyanotic. All four episodes immediately followed excitement or unusual exertion. She had no aura but usually had a sense of oppression beneath the upper sternum just before fainting. She had never injured herself, there had been no twitching of the limbs or the head, no convulsions, and no urinary or fecal incontinence. The pulse rate was counted once while she was unconscious and was said to have been between 60 and 70 per minute. She had not suffered from unusual dyspnea, cough, orthopnea, palpitation, or edema.

The past history was not recorded. At the age of nineteen years she had been told that she had heart disease.

Physical examination showed a pale, undernourished woman, quite tall but weighing only 110 pounds. There was no dyspnea, orthopnea, cyanosis, or engorgement of the cervical veins. The apex impulse of the heart was visible in the sixth left intercostal space in the anterior axillary line. There was a prolonged systolic thrill over the aortic area; no thrill was felt at the apex. The cardiac rhythm was regular and the rate normal. Over the apex the first heart sound was very loud and banging, and continued into a loud systolic murmur; no diastolic murmur could be heard. In the aortic area there was an intense coarse systolic murmur, audible also over the carotid and subclavian arteries. The aortic second sound was extremely faint, and there was a prolonged blowing diastolic murmur along the left sternal border. The position of the apical thrust shifted readily with rotation of the patient's body. The blood pressure was 100/72. The lungs were clear. The liver was not enlarged. There was no edema.

The Wassermann reaction on the blood serum was negative.

The signs were interpreted as indicating rheumatic heart disease with aortic stenosis and insufficiency, mitral insufficiency and possibly mitral stenosis.

One year later she reported that she had not had any fainting spells, but had occasionally noticed pronounced dizziness on walking. While at rest, she felt entirely comfortable. Two months later she lost consciousness while walking along the street and remained unconscious for at least fifteen minutes before she was found. Aside from slight bruises there was no injury. Three weeks later, just after eating dinner, she again lost consciousness. At this time she stated that there had been a sense of slight oppression beneath the upper sternum just before she fainted.

One year later her physician was called to see her because the fainting spells were occurring more frequently. X-ray films of the teeth were secured and showed numerous apical abscesses. All the teeth were removed and three weeks later the physician was informed by the patient's husband that she felt much better. About two weeks afterward she was sitting quietly conversing with her husband, when she suddenly fell from her chair and was dead by the time he could reach her side.

Autopsy was not permitted.

CASE 8.—S. N., a Jewish farmer of fifty-two years, was sent to the New Haven Hospital by his physician for observation and rest. He stated that two years earlier he had suddenly fallen unconscious while running in pursuit of his cattle. He did not know how long he remained unconscious, but was later able to walk slowly to his home, feeling as if he were intoxicated. About one month later he again fainted while running, and was just recovering consciousness two hours later when found by his wife. Within six months he had experienced eight similar episodes, all of them occurring while he was running or doing heavy manual labor on his farm. Upon the advice of his physician, he stopped farm work for five months; he then resumed his work, but noticed great difficulty in walking, especially up hills or up stairs. After walking for only one or two minutes, he had a sensation of oppression beneath the sternum, and increasing dizziness; everything would begin to turn black, and he felt that he would lose consciousness if he did not sit down or lean against a support. For the nine months preceding his admission to the hospital, he had worked very little. He had not suffered from orthopnea, cough, or edema.

His past health had been excellent; he could recall no illnesses.

Physical examination: The patient was well developed and nourished and did not exhibit cyanosis, dyspnea, or venous engorgement while at rest. The apex impulse of the heart was palpable in the fifth left intercostal space beyond the mammary line. There was a distinct systolic thrill in the aortic area, felt best during expiration with the patient leaning forward. No thrill was felt at the apex. The cardiac rhythm was regular, the rate normal. The heart sounds were of poor quality. In the aortic area and over the carotid and subclavian arteries there was a loud, harsh systolic murmur. The aortic second sound was absent. No diastolic murmur was heard over any portion of the precordium. The blood pressure was 120/80. There was moderate sclerosis of the peripheral arteries. There were no signs of visceral engorgement.

A seven-foot roentgenogram of the heart revealed moderate enlargement of the left ventricle. There was no dilatation of either auricle, and the aorta was normal in size and shape. Electrocardiogram showed normal sinus mechanism. The blood Wassermann was repeatedly negative.

The signs were interpreted as indicating aortic stenosis without insufficiency; the etiology was thought to be uncertain.

He remained in the hospital for one month, the only treatment being rest. On several occasions while walking about his room he was forced to stop because of increasing dizziness; he felt sure that he would lose consciousness if he continued the exertion.

He was readmitted to the hospital six months later because of signs and symptoms of congestive heart failure. These had appeared several weeks previously, following an infection of the upper respiratory tract. At this time he displayed the classical signs of heart failure with venous congestion. The physical signs relating to the heart were unchanged except for increased rate. There was moderate improvement as a result of rest and the administration of digitalis, and he was discharged after three weeks, to continue resting at home.

Ten weeks later he was admitted for the third time because of rapidly increasing heart failure. He remained in the hospital for three months; at first there was some response to digitalis and diuretics, but later he became steadily worse, and died. Death did not occur suddenly.

Post-mortem examination: The heart weighed 750 grams. There was an increase in the thickness of the left ventricular wall. The mitral, pulmonary, and tricuspid valves appeared perfectly normal. The aortic orifice, as viewed from above, was narrowed to a minute slitlike opening which would barely admit a small probe; when opened, the aortic orifice measured only 5 cm. in circumference. The valves were greatly distorted, thickened, and calcified. In the sinuses of Valsalva there were

large calcified masses, extending to the valve cusps. The right anterior and posterior cusps were completely fused by calcareous masses. On the margins of all three cusps there were a few very small friable granulations. Microscopic examination revealed a notable increase in the size of muscle fibers of the left ventricle. Throughout the walls of this chamber there was fine diffuse fibrosis in addition to large islands of denser scarring. The orifices of the coronary arteries were patent, and no obstruction could be found in any of their branches.

CASE 9.—F. B. F., a white American housewife of sixty-two years, complained of pain in the left shoulder and down the outer aspect of the left arm as far as the wrist. This was said to have been present for at least twenty years, and was elicited only by physical exertion. For the preceding two years, pain had occurred also over the precordium, often beginning in the left breast and radiating to the shoulder and down the outer aspect of the arm. It had never been experienced beneath the sternum, had never been constricting or tearing in character, never severe enough to make her cease walking, and had invariably disappeared within five or ten minutes, although she continued walking. Six months earlier, she had suddenly fainted while walking along the street. She was unconscious for only about a minute, and upon recovering consciousness felt perfectly well. She consulted a physician who told her she had heart disease; this was her first knowledge that anything was wrong with her heart. She had never suffered from dyspnea, orthopnea, cough, or edema.

Careful questioning about the past history and family history revealed no items of significance.

Physical examination: The patient looked perfectly healthy; her color was excellent; the respirations were entirely normal during rest and quiet activity. There was no venous engorgement in the neck. The size of the heart could not be satisfactorily determined by physical examination; the apex impulse was faintly felt in the fifth and possibly the sixth left intercostal spaces just outside the mid-clavicular line. There was a systolic thrill over the aortic area, also felt over the subclavian arteries; no thrill was felt at the apex. The cardiac rhythm was regular, the rate 80 per minute. In the aortic area there was a harsh, prolonged systolic murmur, transmitted to the carotid and subclavian arteries. The aortic second sound was absent. In a very small area at the left sternal border at the level of the third costal cartilage, a soft short diastolic murmur could be heard. There was a short blowing systolic murmur at the apex. The blood pressure was 184/96. There was moderate arteriosclerosis of the radial, brachial, and retinal arteries. The lungs were normal to percussion and auscultation. The liver was slightly enlarged. There was no edema.

Fluoroscopic examination revealed moderate enlargement of the heart, the increase in size apparently involving only the left ventricle. There was no dilatation of either auricle, and the aorta was of normal size. Electrocardiogram showed normal sinus mechanism, left axis deviation, and slight inversion of the T-waves in Leads I and II. The Wassermann reaction on the blood serum was negative.

The physical signs were interpreted as indicating aortic stenosis and very slight insufficiency; the etiology was thought to be arteriosclerosis, possibly subsequent to rheumatic damage.

During the following year there were repeated episodes characterized by sudden loss of consciousness. These usually lasted about ten minutes and invariably occurred during, or immediately at the conclusion of, such physical exertion as walking along the level or up one flight of stairs. These continued until her physical exertion was practically ended by the onset of congestive heart failure, of which she died two and one-half years after her first visit. Death was not sudden or unexpected. Autopsy was not performed.

CASE 10.—H. H., a white American woman of fifty-eight years, was referred for examination because of fainting spells. Twice within two months she had suddenly lost consciousness while walking along the street; she was unconscious for ten minutes on the first occasion, and about three minutes on the second. For about a year she had noticed slight breathlessness after climbing hills or stairs, but none while walking along the level. She had never had orthopnea, cough, edema, or substernal pain.

She had never had rheumatic fever, chorea, scarlet fever, or diphtheria. There had been frequent tonsillitis in earlier life.

Physical examination: She appeared perfectly healthy. Color and respirations were normal. The apex impulse of the heart could not be seen or felt. There was a distinct systolic thrill in the aortic area; none was felt elsewhere. The cardiac rhythm was regular and the rate normal. In the aortic area there was a very loud, rasping systolic murmur well transmitted to the arteries in the neck. The aortic second sound was extremely faint. There was a very faint short diastolic murmur beneath the upper sternum, audible only when the patient stopped breathing. The blood pressure was 162/96. There was slight sclerosis of the retinal arteries and moderate sclerosis of the radial and brachial arteries.

Fluoroscopic examination revealed moderate enlargement of the left ventricle and increased density of the aortic shadow. There was no dilatation of the auricles. The aorta was normal in size. The electrocardiogram showed left axis deviation; the conduction intervals and ventricular deflections were normal.

The Wassermann reaction on the blood serum was negative.

The physical signs were regarded as those of aortic stenosis with slight insufficiency. It was thought that the lesion was probably arteriosclerotic but possibly rheumatic, or a combination of the two.

For several months she was free from syncope, then for many weeks noted dizziness on walking; this would disappear upon cessation of the exertion. After a few months, however, she began to have complete loss of consciousness associated with walking or with other forms of physical exercise. About eighteen months after her visit she became unwilling to go out of doors because the effort of walking even very short distances often caused syncope, which lasted from three to ten or fifteen minutes. On several occasions she fell unconscious on the street even though for several preceding days she had been able to walk without difficulty. She did not develop congestive heart failure. Almost exactly two years after she came under observation, she walked upstairs to get her hat, preparatory to starting on a motor ride. Her husband and sister heard her fall to the floor, and rushed at once to her; she was completely unconscious, and died within several minutes.

CASE 11.—A white, married, American salesman sixty years of age was admitted to the New Haven Hospital in May, 1930, because of dizziness, palpitation, and dyspnea. He had suddenly become dizzy and lost consciousness for the first time nine months previously, and had then felt perfectly well until one month before admission. At that time he had a typical paroxysm of nocturnal cardiac dyspnea, relieved promptly by the administration of morphine.

The past and family histories disclosed no items of apparent importance.

Physical examination showed obesity, moderate dyspnea and orthopnea, slight engorgement of lungs and liver. The heart was not enlarged as judged by physical examination, there was gallop rhythm and a faint systolic murmur at the apex. There was no note of a basal systolic murmur. The blood pressure was 100 to 130 systolic, 60 to 70 diastolic. The prostate gland was enlarged. There was no edema. Examinations of the blood, urine, and stools yielded normal findings; the chemical components of the blood and the renal function tests were likewise normal. Electrocardiograms on several occasions showed moderate physiological tachycardia, left axis deviation, and occasional ventricular premature beats. The Kahn test on the blood serum was negative.

The clinical diagnosis was arteriosclerotic heart disease with early congestive heart failure. Treatment consisted of rest in bed, limitation of fluids, and the administration of sedatives and of digitalis; after two weeks he was perfectly comfortable and was discharged.

He reported at intervals of one to three months at the Cardiac Clinic of the New Haven Dispensary from June, 1930, until October, 1932; it was not until this latter date that he first came to the attention of one of us. He stated that during the two and a half years since his discharge from the hospital, he had not suffered from the symptoms of congestive or anginal heart failure, but that his entire difficulty had consisted of loss of consciousness associated with walking. A review of his written records showed that he had fainted sixteen times during that period, always during or immediately at the cessation of walking. At times he could walk four or five blocks before losing consciousness; at other times, he would faint after walking less than a half block. The time of day, the season, the temperature and humidity, the presence of food in the stomach, his feeling of well-being or the reverse, all appeared to be without effect; he stated that he could induce fainting at any time by walking a short distance. His first abnormal sensation was one of great emptiness in the upper abdomen and lower chest; this extended rapidly upward to the neck, he became dizzy and lost consciousness within a few seconds of the first warning. The period of total unconsciousness lasted from five to fifteen or twenty minutes as a rule; this was followed by one or two hours of weakness, after which there was complete recovery. So long as he refrained from walking he felt perfectly well, and could perform his regular duties as a hardware salesman.

Examination at this time disclosed no findings of interest other than those relating to the heart. The heart's apex lay in the fifth left intercostal space, directly in the mammillary line. No thrill could be felt with certainty at the apex or base. The rhythm was regular, the rate normal. In the aortic area there was a harsh but not very intense systolic murmur, typical in all respects of that usually associated with aortic stenosis, and well heard over the subclavian and carotid arteries. The aortic second sound was absent. No diastolic murmur could be heard by any of several examiners. The blood pressure was 150/98. There were no signs of venous congestion. It was our impression that the patient had aortic stenosis of the calcareous type, without signs of aortic insufficiency, and that the syncope was in some way related to the narrowing of the aortic orifice.

Treatment was purely symptomatic; at various times he took digitalis, metaphyllin and quinidine, but without clear evidence of benefit. He continued to have occasional syncope, always during or immediately after walking, with a single exception. On that one occasion he was sitting quietly in a chair, and leaned forward to place a small box over a plant. As he sat up again, he realized that he was about to faint, but was able to walk about fifteen feet to a couch, and fell unconscious upon it. Following this episode, however, he could sometimes walk for an hour twice a day for some weeks without losing consciousness, only to faint unexpectedly after walking less than a hundred yards. Altogether, he had about thirty episodes during the period from October, 1930, until May, 1933.

During part of this time, we had tried vainly to persuade him to precipitate an attack in the cardiographic laboratory by means of deliberate exercise, but he was afraid that each episode might prove fatal, and was unwilling to provoke one voluntarily. However, in May, 1933, he consented to permit observations, of which an abbreviated protocol follows:

Unfortunately, the following observations are incomplete and unsatisfactory for several reasons: The room was in semidarkness most of the time in order to secure electrocardiograms, and the noise of his stertorous respirations and the convulsive

movements of the arms made it difficult to secure satisfactory curves and to hear the heart sounds. A preliminary electrocardiogram of the usual three leads was secured. The time is recorded in minutes.

0 Preliminary electrocardiogram completed (Fig. 1*A*).

1¾ The patient started walking from the laboratory into the adjacent room, a total distance of about 20 feet. He swung his arms vigorously all the time in order to increase the exertion.

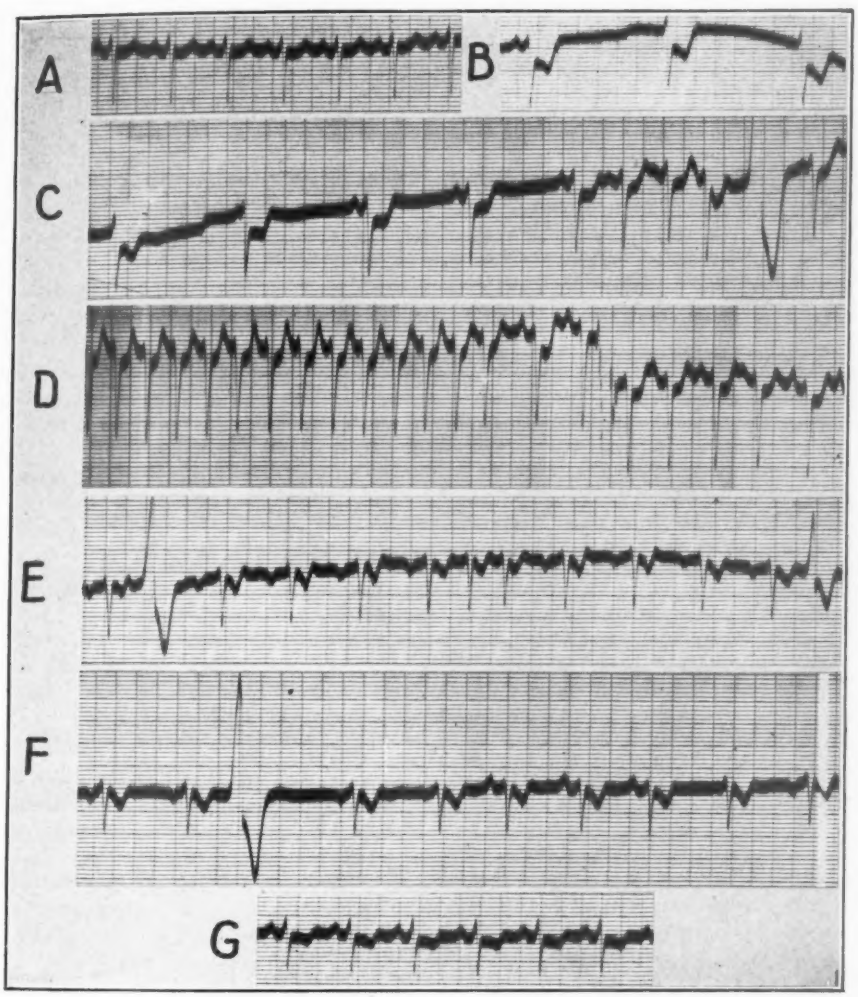

Fig. 1.—Electrocardiograms of Case 11. All records are of Lead II. Time is in fifths of a second.

A, Before exercise.

B, Just after onset of syncope. Nodal rhythm, bradycardia, and marked depression of origin of T-wave.

C, A few seconds after *B*; patient completely unconscious. Return of sinus mechanism and appearance of ventricular premature beats.

D, A half minute after *C*. Paroxysmal tachycardia, rate 200 per minute.

E, About three minutes after *D*; patient conscious. Auricular and ventricular premature beats and inversion of T-wave.

F, Ninety seconds after *E*; patient fully conscious. Shifting pacemaker. Ventricular premature beats.

G, Four minutes after *F*. Premature beats have ceased. T-wave is apparently returning toward normal.

For more complete description see the text.

5 At the end of the seventh trip (a total distance of approximately 280 feet) his color was grayish white, and he sat on the edge of the couch, stating that he was fairly certain he was about to lose consciousness. Unfortunately, an electrocardiogram was not secured at this moment; it was delayed in the belief that further exercise might be necessary. Within a few seconds, however, he lay down on the couch, his eyes rolled upward, the breathing became stertorous and quite loud. As soon as possible an electrocardiogram was secured; it began at the sixth minute. The record was terminated in the middle of Lead II by convulsive movements of the patient's arm which made it impossible to keep the string shadow focused on the camera. The rate in the earlier portion of the record was approximately 70 per minute and irregular; in the latter portion it was about 50 per minute and regular. Lead I showed ventricular escape and nodal rhythm, but the ventricular deflections were unaltered. Lead II showed a continuation of nodal rhythm and a profound change in the T-wave which had its origin below the zero level and turned sharply downward (Fig. 1*B*). The blood pressure during the period of slow rate was 124/80. After a few seconds of waiting, another portion of Lead II was secured which showed the return of normal mechanism, then a sudden increase in rate and the appearance of ventricular premature beats (Fig. 1*C*). There was now complete loss of consciousness with deep, noisy respirations, occasional movements of the right arm and head, and slighter, less frequent movements of both legs.

8 This record (Fig. 1*D*) was started at the eighth minute, about thirty seconds after the conclusion of the preceding curve. It showed simple paroxysmal tachycardia with a rate of 200 per minute; there was a change to sinoauricular tachycardia about the middle of the record. At this moment the patient began to sigh and muttered a few words, but it was clear that he had not fully recovered consciousness. Blood pressure had risen to 190/100.

11 The patient seemed to be fully conscious but continued to sigh loudly and to roll his head impatiently from side to side. The rate of the heart was slightly above normal, and there were occasional premature beats. Electrocardiogram showed inversion of the auricular waves and continued inversion of the T-wave which did not, however, arise so far below the base line. There were premature beats arising in both auricles and ventricles (Fig. 1*E*).

12½ Patient more quiet. Premature beats less frequent. Blood pressure 160/90. Electrocardiogram (Lead II) shows P- and T-waves still inverted. (Fig. 1*F*).

14 Cardiac rate and rhythm normal. Blood pressure 156/90.

16½ Electrocardiogram (Lead II) shows normal mechanism with slight depression of the S-T interval and T-wave (Fig. 1*G*).

17 All three leads of electrocardiogram taken. In comparison with those obtained before exercise, there were a few minor changes. The ventricular deflections were smaller in all three leads of the second record; the T-wave in Lead I was more deeply inverted than in the preexercise curves; and in Lead II the S-T interval was depressed in the second record, although the T-wave in this lead was upright in the first.

18 Cardiac rhythm regular. Blood pressure 126/90.

23 The patient said he felt very warm, but was perspiring less than usual after recovering consciousness. He thought this episode was typical in all respects but less severe than most, which he ascribed to the fact that he was able to lie down as soon as he felt any discomfort.

30 He felt just as usual after an attack. (He remained at rest for another hour and then was taken to his home by automobile.)

Comment.—It seems clear that electrocardiograms should have been taken as soon as the patient felt uneasy rather than after the loss of consciousness. Auscultation of the heart was practically valueless for a time because of the noisy respirations and the patient's groaning. The electrocardiograms revealed several changes that are possibly of importance:

(1) A considerable reduction in the rate of the heart.
(2) The onset of A-V nodal rhythm.
(3) A remarkable change in the T-wave in Lead II, which arose from the ascending limb of the S-wave considerably below the zero line.
(4) Occurrence of many ectopic beats, shortly followed by simple paroxysmal tachycardia at a rate of 200 per minute.
(5) Conspicuous and deep inversion of the T-wave in Lead II, different from that mentioned in (3), which gradually became less and in the final curves was manifested as moderate depression of the S-T interval.
(6) Frequent changes in position of the pacemaker after the subsidence of the tachycardia.

Repeated attempts were made to induce this patient to return for a repetition of the entire procedure, but he refused. Some months after these observations had been made there appeared the splendid paper by Weiss and Baker,[21] which first made us suspect the possibility of hyperactivity of the carotid sinus in this and similar cases.

From May until November, 1933, the patient had only three or four syncopal attacks, and on most days was able to walk for at least two hours without symptoms. On November 8, he felt as well as usual, and was walking about in his yard, but in the late afternoon he came indoors, telling his wife that he was about to faint. He was able to reach his bed before losing consciousness, and the attack seemed to his wife exactly similar to all previous ones. After about ten minutes he had recovered sufficiently to smile and speak to her; within several minutes, however, another similar episode began and progressed to its usual conclusion. Once more he smiled at her as he regained consciousness, but almost immediately a third syncopal attack began, and he died within five minutes, just as his physician reached the room. His wife and daughter, who had witnessed most of his attacks, were emphatic in stating that the three of this day were precisely similar in appearance to all the earlier ones; the changes in color and in breathing, the convulsive movements, the duration, the slow recovery were just as they had been on previous occasions.

Autopsy was performed at the New Haven Hospital about four hours later. The heart was moderately enlarged, its weight being 480 grams. There was extreme stenosis of the aortic orifice with dense calcification of all cusps which were converted into a single firm mass. The orifice was reduced to a narrow slit about 2 mm. wide and 6 mm. to 7 mm. long. There was moderate hypertrophy of the left ventricle, with but little dilatation. The mitral, tricuspid, and pulmonary valves were normal in appearance. The orifices of the coronary arteries were patent, and no evidence of occlusion could be found in any branch. Microscopically the heart showed hypertrophy of the muscle fibers with very little fibrosis. Both carotid sinuses were removed, and no abnormality could be detected grossly or microscopically.

DISCUSSION

Of these eleven cases, it seems reasonably certain that the first seven had the rheumatic type of heart disease; in the remaining four cases, the etiology must be regarded as less certain. These four presumably

TABLE I

CASE	SEX	AGE	TYPE OF HEART DISEASE	AORTIC INSUFFICIENCY	MITRAL STENOSIS	CONGESTIVE HEART FAILURE	SYNCOPE	INDUCED BY	DURATION	TYPE OF DEATH	REMARKS
1	F	45	Rheumatic	+	+	0	0			Sudden	Intraventricular heart-block.
2	M	37	Rheumatic	+	+	Dyspnea only	0			Sudden	
3	M	41	Rheumatic	+	+	Advanced	0			Sudden	Anginal failure some months earlier. Intraventricular heart-block (slight).
4	M	40	Rheumatic	+	0	Advanced	0			Sudden	Autopsy performed.
5	F	35	Rheumatic	+	+	Slight	0			Sudden	
6	M	58	Rheumatic	+	+	Moderate	0			Sudden	Closure of aortic orifice by thrombus (autopsy).
7	F	30	Rheumatic	+	?	0	Many	Exertion or eating	3 to 30 minutes	Sudden	
8	M	53	? Rheumatic	?	0	None at time of syncope	Many	Exertion	Minutes or hours	Progressive heart failure	Autopsy performed.
9	F	62	Arterio-clerotic	Slight	0	0	Many	Exertion	10 minutes	Progressive heart failure	
10	F	58	?	Slight	0	0	Many	Exertion	3 to 10 minutes	Sudden	
11	M	60	?	0	0	0	Many	Exertion	5 to 20 minutes	Sudden	Autopsy performed.

belong in the group that has been discussed at some length by numerous observers[2, 11, 12, 14, 17, 18]—the group composed of elderly people who present clinical signs of aortic stenosis with or without slight aortic insufficiency and who, at post-mortem examination, show moderate or extreme calcification of the aortic valve cusps and no disease of the mitral valves. After a consideration of all the known factors relating to etiology, most of the above authors have reached the conclusion that the cardiac lesions are probably rheumatic in type, with subsequent arteriosclerotic changes, but recognize that the question of etiology has not been answered with entire satisfaction. In the present paper we refer to this type of aortic stenosis as arteriosclerotic or calcareous for the sake of uniformity and brevity, but it is our belief that the etiology is yet uncertain. Of our first seven cases, six patients were forty-five years of age or less, and all presented unequivocal clinical signs of rheumatic heart disease. Even if the remaining four cases be regarded as also primarily rheumatic, it is quite possible that the signs and symptoms were not due to the original lesions, but rather to calcareous changes that occurred only after the passage of many years. The point might seem of purely academic interest were it not for a possible difference in the symptomatology of the two groups. In the cases here reported, for instance, sudden death occurred in all of the seven rheumatic patients and syncope in but one of them. Campbell and Shackle[16] also found a higher incidence of syncope in the cases of atheromatous aortic stenosis than in those of rheumatic type.

A brief summary of the significant facts relating to these eleven patients is contained in Table I. It will be observed that nine died with extreme suddenness, and four of these had no heart failure at the time; another (Case 2) had no symptoms except slight dyspnea on exertion, and was apparently better than he had been for many months. The remaining four (Cases 3 to 6) had slight or advanced congestive heart failure but were no worse on the day of death than they had been for days or weeks; in fact, one of them was apparently improving steadily. Autopsy in three cases failed to reveal any adequate cause for the sudden death; in one the cause was thought to be complete thrombotic closure of the narrowed aortic orifice. In five of the eleven patients, repeated fainting spells constituted the chief symptom; in all of these, syncope occurred chiefly or only in association with physical exertion. It has already been mentioned that four of these five had the calcareous type of aortic stenosis. One of them lived for approximately two years after the onset of syncope, two for about three years, and one for six years. Three of these five died suddenly, one of the rheumatic and two of the arteriosclerotic group.

Such, briefly, are the known facts relating to these patients. The problems which they present are the two indicated in the title of the paper: why are they subject to sudden prolonged loss of consciousness while

carrying on slight physical exertion, and why do many of them die with extreme suddenness when apparently quite well? It is perhaps impossible, on the basis of the imperfect and inadequate evidence now available, to arrive at an acceptable answer, but the possibilities may be indicated briefly. Those relating to the suddenness of death will be considered first.

Sudden Death.—Embolic closure of a large artery (coronary, pulmonary, or cerebral) is one of the first possibilities that comes to mind in cases of sudden death, but there are many reasons for believing it inacceptable as an explanation in the patients now under consideration In most of these, auricular fibrillation is not present, and aortic stenosis in itself does not provide any unusual opportunity for the formation of intracardiac thrombi. Moreover, death caused by large emboli is seldom as instantaneous as that in the patients here presented; almost invariably it is delayed for at least several minutes after the occurrence of the vascular accident, and in many instances the patients give some indication of the location of greatest distress by clutching at the chest, gasping for breath, etc. Apparently the patients who have aortic stenosis die in seconds rather than minutes, and the abruptness of the termination strongly resembles that sometimes observed in anginal patients or in those who have recently sustained myocardial infarction. A final, and in itself conclusive, argument against the acceptance of the embolic theory is found in the fact that post-mortem examination has not revealed such an embolus in any reported case, and it is impossible to believe that one large enough to cause immediate death could be invariably overlooked by pathologists.

Sudden occlusion of the small aortic orifice by a blood clot formed in situ is a possibility that would seem incredibly remote had it not been demonstrated in one case previously reported[9] and in Case 6 of the present group. It would seem almost impossible that a blood clot could form in an orifice constantly exposed to the full force of left ventricular contraction, and it is probable that in both of the known cases there was extreme weakness of the left ventricle at the time the thrombus formed. There is of course the possibility that in both the clot was a post-mortem one and had no causal relation to the sudden death. Even if one accepts these two as conclusive, however, it remains true that the great majority of recorded cases have failed to show thrombotic closure of the aortic orifice, and this must be regarded as a rare event.

Interference with the coronary circulation by distortion of the orifices of these arteries, with subsequent thrombotic closure of a large branch, might explain the suddenness of death in some instances, but in most it cannot be regarded as the explanation because careful search post mortem in a number of cases has failed to reveal any such lesion. Moreover, increasing experience with patients who have suffered coronary arterial thrombosis indicates that death from this cause is seldom in-

stantaneous at the time of the initial closure; it is far more liable to occur after a few minutes, several hours, or several days.

That abrupt death cannot be satisfactorily explained on the basis of mechanical narrowing of the aortic orifice is sufficiently indicated by two considerations. It has long been known that patients with extreme stenosis of this orifice may live for months or years in comparative comfort and even carry on fairly strenuous physical activity; this is a matter that has received widespread comment. Moreover, many patients with aortic stenosis have died not abruptly, but in the usual slowly progressive fashion characteristic of congestive heart failure, even though the aortic opening was much smaller than in others who died suddenly. If the mechanical narrowing were important, one would expect a certain parallelism between extreme degrees of stenosis and the tendency to die suddenly. In some of the cases reported by Margolis and his associates the degree of stenosis was so slight that it was not recognized clinically, yet death occurred with extreme suddenness.

It is possible that the size of the heart may be of some importance in determining whether or not sudden death will occur. It is certainly true that in the group here reported enlargement of the heart was much greater in those patients who died suddenly than in the others. If one adopts the view that death in such cases is due to the onset of ventricular fibrillation, there are observations suggesting that this is more liable to occur in large hearts than in small ones.[19, 20] Whether or not this suggestion applies to the cases reported by Cabot, Margolis, and Willius cannot be known because the degree of enlargement of the heart is not stated by these authors.

There is as yet no clear proof that the cause of death in these patients is the same as that of syncope; it is at least conceivable that they are due to entirely separate and unrelated causes, and do not represent simply major and minor reactions to the same stimulus. It is natural and proper, however, to assume for the moment that syncope and sudden death may owe their origin to the same mechanism, and the events in our Cases 7, 10, and 11 would appear to lend strong support to this view, for in all of them death occurred suddenly after a long series of syncopal attacks, and one of these patients died during a seizure which seemed typical of all its predecessors. The evidence afforded by this one case is actually of the greatest value, for the circumstances of the last few moments of life are known accurately, and he had been the subject of careful preceding observations. To state that death occurred in one instance during, or at the termination of, a typical syncope is to imply that a common cause might have been responsible for both loss of consciousness and cessation of life.

This implication leads directly to the consideration of hyperactivity of the carotid sinus reflex as a cause of death—a possibility that was un-

recognized by us during the study of our first ten cases. The fainting in many of these patients is apparently quite similar to that attributed by numerous observers to this reflex, and the whole series of antemortem observations in Case 11 can be duplicated in several of the cases reported in the admirable and careful study of Weiss and Baker.[21] There is, however, one major difficulty in accepting hyperactivity of this reflex as the cause, namely, that death has not occurred suddenly in any reported patients known to have hyperactivity of this reflex. Weiss[22] states that none of the patients observed by him have died in a manner that could be attributed to the carotid sinus mechanism, and that the spontaneous syncope in their patients was of brief duration.

We are not prepared as yet to acknowledge that this difficulty is sufficient to exclude the carotid sinus reflex as a cause of death, for on theoretical grounds it would seem highly probable that death might result from a mechanism capable of causing profound vasomotor changes and extensive alterations in the cardiac mechanism. Further observations alone can solve the problem, but in the present state of our knowledge it seems well to suggest that death in the present group of cases might have been due to hyperactivity of the carotid sinus reflex in patients who had aortic stenosis also.

From this brief consideration it seems reasonably clear that the cause of sudden death in a great majority of these patients is not to be found in embolism, thrombosis, or mechanical narrowing of the aortic orifice. It is our belief that the cause is probably either (a) the combination of aortic stenosis and hyperactive carotid sinus reflex, or (b) the same mechanism that terminates life in many patients who have anginal heart failure or who have sustained recent thrombosis of a coronary artery. It seems to be the prevailing opinion that this mechanism is dependent upon the onset of ventricular fibrillation or upon a depressor reflex other than that involving the carotid sinus, but conclusive evidence of its precise nature is yet to be obtained.

It will be observed that six of our first seven patients had mitral stenosis in addition to aortic stenosis and insufficiency, and the question naturally arises as to its possible relation to the sudden death. That this lesion is almost certainly unimportant in the group of cases now under discussion is indicated by two facts: (1) In cases of mitral stenosis and insufficiency without evidence of aortic valve damage, sudden death during the maintenance of regular cardiac rhythm is exceedingly rare. When auricular fibrillation has been added, unexpected and fairly rapid death occurs not infrequently as a result of cerebral or pulmonary embolism. In a fairly extensive experience with cases of mitral stenosis, we have never known an example of the type of death discussed in this paper. Cabot[2] lists two patients of his 107 cases of mitral stenosis as having died suddenly, but the details of these cases show that one patient lived for five days after the onset of unexplained coma, and the other

lived for some hours after becoming unconscious; this is not the type of "sudden" death with which we are here concerned. (2) The majority of recorded cases of sudden death have been in patients who did not have mitral stenosis as shown by autopsy; this was true of all those reported by Cabot and by Margolis, and of three cases (Nos. 4, 6, and 11) of the present group.

A more important question, and one that will inevitably be asked, is why we are warranted in assuming that the sudden death in these patients is related to the aortic stenosis rather than to the aortic insufficiency. It is difficult to answer this with convincing certainty, but there are several reasons which appear to indicate that it is the obstruction rather than the regurgitation which is the important factor. It is realized that many observers during the past century have referred to the suddenness of death sometimes associated with aortic insufficiency or, more frequently, with the indefinite lesion designated "aortic valve disease." It is often impossible, in the case of the earlier writers, to ascertain whether the lesion in their cases was stenosis or insufficiency or both. Even when it is clear that aortic insufficiency was present without stenosis, it is probable that in many instances the etiology was syphilis. In the absence of more precise studies and more detailed descriptions, one cannot be unduly influenced by general statements without known foundation; we have been unable to find any satisfactory evidence to warrant the belief that nonsyphilitic aortic insufficiency without stenosis is a cause of sudden death or frequent syncope. It is our belief that sudden death of patients with aortic insufficiency without stenosis occurs with extreme rarity except in one clearly defined pathological state, namely, syphilitic aortic insufficiency. That it does occur at times in this condition is undoubtedly true, but its frequency has possibly been exaggerated. It is pertinent to indicate in this connection that no patient of the present group had any evidence of syphilis; that is true also of the cases reported by Cabot, by Margolis and his collaborators, and presumably, though not certainly, true of the cases reported by Willius. Three patients of the four cases of sudden death reported by Campbell and Shackle[13] did not have syphilis.

If one considers examples of acquired aortic insufficiency due to all causes other than syphilis, it is more difficult to make a positive statement. It seems probable that there are but two other groups; the rheumatic group, in which the aortic lesion is almost always associated with mitral stenosis, and the arteriosclerotic-hypertensive group. The rheumatic group is discussed later in some detail and need not be mentioned further at this point. The other group is far smaller and less well defined; its existence is actually denied by some competent observers, but there can be no question that a small proportion of middle-aged or elderly people who have arteriosclerosis with or without hypertension, do present clinically an unmistakable diastolic murmur at the base of the heart and

beneath the sternum. Very often the usual peripheral vascular signs associated with aortic regurgitation are absent, but sometimes these too are present. Signs of mitral stenosis are entirely lacking.* The group is too small to be of importance, and we have no figures comparable with those given below. Of the last 123 patients dying in this hospital as a result of the arteriosclerotic type of heart disease, only five had physical signs of aortic insufficiency during life. None of these died suddenly.

The fact that those who have reported previous cases have emphasized the stenosis rather than the insufficiency as the cause of sudden death is probably quite without importance, because the diagnosis in their cases was based on autopsy findings; the anatomical lesion in such patients is stenosis, and the presence of regurgitation during life is deduced, not demonstrated. Both Cabot and Margolis state that insufficiency *must* have been present in their cases; the absence of physical signs of this condition during life is a point of no value whatever in view of the fact that signs of aortic stenosis were not found during life in many of Cabot's cases, and were described in only two of Margolis' cases. Granting that their patients had clear post-mortem evidence of stenosis and insufficiency, it becomes impossible to assert, on the basis of these cases alone, that death was due to one rather than to the other. Evidence must be sought in analogous cases, and this is attempted briefly in the paragraphs that follow.

Conclusive observations bearing upon this point could be obtained readily if there were comparable groups of patients having "pure" aortic insufficiency and "pure" aortic stenosis. The first group is available in those who have syphilitic involvement of the aortic valves, but the second is so small as to be negligible, because almost all patients with aortic stenosis have insufficiency also. It has therefore seemed to us that the most decisive evidence was to be derived from a comparison of two groups of patients, the first having mitral stenosis and aortic insufficiency, the second having these same lesions plus aortic stenosis. In such a comparison, we are dealing with two groups as nearly identical as possible with respect to age, sex, etiological factors and anatomical damage; the only important difference between them is the presence of aortic stenosis in one group and its absence from the other. If narrowing of the aortic orifice is actually the important lesion in relation to sudden death, there should be a notable difference in the two series.†

*We do not wish to be understood as expressing the opinion that aortic insufficiency in these patients is due to arteriosclerosis. We regard the etiology as uncertain, realizing that it may be rheumatic.

†We are in agreement with Cabot that rheumatism tends to cause stenosis (as well as insufficiency) in the case of both mitral and aortic valves, and recognize that it is merely a later stage of a single disease process. And while it is clear that aortic stenosis is frequently overlooked during life, even by careful examiners, we are not wholly in agreement with his statement that physical signs of rheumatic aortic insufficiency justify the assumption that aortic stenosis is present also. His rule could doubtless be applied with greater accuracy to hospital patients with congestive heart failure than to the large group of living patients who have no symptoms referable to the heart. It seems clear that there must be a stage in the pathological process when insufficiency is present without demonstrable narrowing of the orifice.

We have therefore reviewed our records, both of hospital and of private cases, and have divided them into two such groups. We have been careful to exclude all cases of syphilitic heart disease, all cases of mitral stenosis without signs of aortic involvement, all cases of aortic lesions without signs of mitral involvement, and all cases among elderly people having arteriosclerosis and hypertension, in which the etiology of the heart disease might be questioned. During the period represented by the eleven cases here reported, we have observed a total of 108 cases in Group I (mitral stenosis and aortic insufficiency), and 64 cases in Group II (mitral and aortic stenosis and insufficiency). Of these, 30 patients are known to have died in Group I, and 36 in Group II. Not one of the deaths in Group I was of the sudden, unexpected type, while 9 in the other group were of this type (the nine cases reported in the present paper). One patient in Group I died quite rapidly, but this patient had subacute bacterial endocarditis and had suffered repeated embolic accidents; the clinical signs preceding death were those of cerebral embolism, and this diagnosis was confirmed by autopsy.

While the evidence with respect to this point cannot be regarded as absolutely conclusive on the basis of such a small number of cases, it seems nevertheless to lend strong support to the belief that aortic stenosis is the most important lesion predisposing to unexpected and practically instantaneous death. We have already indicated our agreement with the opinion that acquired aortic stenosis without insufficiency is a relatively rare condition, and the above statement should not be regarded as necessarily applying to this small group. It is perhaps clearer to say that in our opinion sudden death is unlikely to occur in cases of rheumatic heart disease without aortic stenosis, but is quite liable to occur in rheumatic heart disease with aortic stenosis, as well as in the older patients with aortic stenosis of the calcareous type.

Syncope.—The consideration of syncope and its probable cause in these patients is rather unsatisfactory. We have been unable to find any study of this symptom in relation to aortic stenosis, and but one detailed report of a case which falls clearly into the group now under discussion. In that case, reported by Smith,[15] the close and invariable association of transient syncope with physical exertion seems, at first glance, sufficient to warrant the explanation that he gives, namely, temporary cerebral anemia due to inability of the left ventricle to force sufficient blood through the narrow aortic orifice. In three of our five cases it is tempting to advance a similar reason, but there are several characteristics of the syncopal attacks that are not satisfactorily explained on this basis. In the first place, syncope occurred in four of our patients during quiet walking along a level street, and, what is particularly significant, occurred only infrequently. These patients could walk quite freely most of the time without any disturbance, but occasionally would lose consciousness without warning. In the second place, one of our patients

(Case 7) sometimes lost consciousness when she was standing or sitting; this occurred more often just after meals, but sometimes hours later. In the third place, it is difficult to understand why cerebral anemia dependent upon exertion should produce unconsciousness lasting for thirty minutes or even for several hours. In only one of our five cases (Case 8) was there any relationship between the severity of the physical exertion and the occurrence of syncope; in the other four, fainting was just as liable to occur after slight as after more strenuous exertion. It seems clear that exertion is an important factor in most cases, but it is far from certain that it is the only one.

That the loss of consciousness in these patients is due in all likelihood to cerebral anemia seems evident enough to require no extended argument; in none of them was there any suspicion of epilepsy; in none have generalized convulsions ever been observed. Transient complete heart-block, with Stokes-Adams attacks during the maintenance of the block, is clearly inadequate to explain the symptoms; the loss of consciousness is far longer than that in Stokes-Adams seizures; the electrocardiogram between syncopal attacks has shown normal mechanism in four of our five cases and in the one reported by Smith; and in at least two instances the heart rate has been counted while the patient was unconscious, and it was but moderately reduced.

Can the syncope be regarded as similar to that occurring in circumstances attended with considerable emotion—the fainting of people who witness gruesome accidents, who see the withdrawal of blood or surgical operations for the first time—the so-called vasovagal syncope? It seems highly doubtful, because the inciting cause in these patients appears to be physical exertion rather than an emotional influence, and because the duration of unconsciousness is far greater than in vasovagal syncope.*

Transient ventricular fibrillation as a cause of the fainting is rendered unlikely by several observations: the almost invariable association with effort, the long duration of unconsciousness, the absence of significant cardiac symptoms between the episodes of fainting, and the frequent repetition of syncope in some cases for long periods of time. Our present knowledge of ventricular fibrillation scarcely permits the assumption that it could manifest itself in this fashion repeatedly over a period of six years, as in our Case 7, or three and a half years as in Case 11.

Hyperactivity of the carotid sinus reflex, already discussed briefly as a possible cause of sudden death, would seem to be even more likely as a cause of the syncope. From a physiological standpoint the circumstances attending the loss of consciousness in the cases here reported are such as to justify the assumption that the sinus was stimulated by the rise of pressure in the carotid artery due to exertion. There is reason to believe that the effects of this normal stimulus would be similar in

*Lewis[20] suggests that the vasovagal seizures may be set up through the same central and efferent mechanism which takes part in the carotid sinus reflex.

type to those following artificial stimulation; these have been lucidly portrayed by Weiss and Baker[21] and need not be discussed at this point further than to indicate that faintness, dizziness, loss of consciousness, and convulsive movements are among the most constant symptoms resulting from direct artificial stimulation. The episodes of fainting in our patients appear to be similar to those reported as occurring after such stimulation of the carotid sinus in normal individuals, and the entire series of events in our Case 11 may be duplicated in several of those reported by Weiss and Baker.* There are, however, two obvious objections to immediate acceptance of hyperactivity of this reflex as the cause of fainting: one is that syncope due to deliberate stimulation of the sinus is usually of brief duration, whereas in several of our patients it lasted for a long time; the other is that the only instances of fainting of this type (occurring in association with moderate exertion, in the absence of such causes as organic disease of the central nervous system, epilepsy, anemia, marked hypotension, great physical weakness, emotional disturbances, etc.) observed by us in the past several years have been in patients with aortic stenosis. The second objection is probably more apparent than real, and further experience will doubtless remove it, although it is conceivable that stimulation of the carotid sinus reflex may occur more readily and lead to more profound and lasting effects in patients with aortic stenosis than in others. As to the first objection, we recognize that our statements about the duration of unconsciousness are open to question; we have relied upon the observations of relatives of the patients, and these may have been inaccurate. Of our five cases, the syncope was of relatively brief duration in three, and in the other two also most of the time, but in these two the unconsciousness is said to have lasted from thirty minutes to two hours on several occasions. However, even if this statement be accepted as accurate, it seems to us probable that the duration of unconsciousness might well be longer in patients whose aortic orifice is greatly reduced in size, for this would tend to lessen still further the cerebral blood supply, already reduced by vasoconstriction.

The evidence as a whole is not absolutely conclusive, but is such as to lead us to suggest that hyperactivity of the carotid sinus is the probable cause of the syncope in patients who have aortic stenosis. Direct stimulation of the carotid sinus in individuals similar to those recorded here will supply much evidence; it is unfortunate that this was not performed in our patients, but we were not familiar with the effects of this procedure in man until our last patient was under observation, and he refused to submit to it.

It is possibly worthy of note that of the five subjects who had syncope, only one presented the clinical signs of free aortic regurgitation.

*It is not clear in their cases how close was the association between physical exertion and syncope; of the twelve cases of spontaneous fainting, exertion was apparently related in three, not related in three, and questionable in six.

From a perusal of cardiovascular literature, both old and recent, one gains the impression that this lesion and this symptom are often and causally related in the minds of physicians. We have repeatedly encountered references to "the syncope of aortic valvular disease," "the fatal syncope of aortic regurgitation," and many writers have explicitly stated or have inferred that syncope is a symptom of aortic insufficiency. We believe this to be incorrect, and while we cannot categorically deny it, we wish to question the accuracy both of the statements and of the implications. In the few years that we have been especially interested in aortic valve lesions and the associated symptoms, we have sought assiduously for evidence that patients with aortic insufficiency of the rheumatic or arteriosclerotic type are more prone to syncope than are normal individuals or those with mitral valve lesions. We have found no such evidence, either in our own experience or in the reports of others; in more than two hundred consecutive cases of rheumatic aortic insufficiency, usually combined with mitral stenosis, we have found a history of fainting only in those patients who had aortic stenosis also. Lewis,[23] among others, has warned against the too frequent assumption that symptoms occurring in the course of a chronic disease are due to that disease, when they might well arise from independent causes. The occurrence of syncope in patients with aortic insufficiency should not be attributed to the valve lesion until more careful and detailed studies have shown that such a relationship actually exists. The mere statement that it occurs in such patients is irrelevant; careful studies of large groups must show conclusively that the incidence of fainting in these patients is considerably higher than in normal individuals who are otherwise strictly comparable, and higher than in patients with other valve lesions and other types of heart disease, before a causal relationship can be inferred. If the fainting in vasovagal syncope and in the patients here reported is due to the carotid sinus reflex or to a reflex involving the same central and efferent mechanism,[23] it may well prove to be true that the incidence of syncope in cases of aortic insufficiency is very low. It is our present belief that there may be a higher incidence in those with aortic stenosis, but this also may prove to be erroneous. The entire subject of syncope must be restudied in the light of recent physiological discoveries; at the moment we can only point out that there is inadequate evidence to justify the belief that syncope is often a symptom of aortic insufficiency.

SUMMARY

We have reported a group of eleven patients who presented typical signs of stenosis of the aortic orifice; seven of these were of the rheumatic type and four of the arteriosclerotic or calcareous type. Nine died with extreme suddenness when they appeared to be in their usual health, and four did not have heart failure at the time. Post-mortem

examination failed to reveal an apparent cause for the sudden death in three cases; in one, the narrowed aortic aperture was completely closed by a thrombus thought to have formed during life.

Five of the eleven patients were subject to sudden and unexpected loss of consciousness associated with slight or strenuous physical exertion. In three of them the unconsciousness lasted from three to ten minutes; in the other two for much longer periods. Three of those subject to syncope died very suddenly and the others of progressive heart failure.

The possible causes of sudden death and of syncope, and their possible relationship to aortic stenosis, are discussed briefly. The present evidence does not justify final conclusions, but it is suggested that sudden death may be due to hyperactivity of the carotid sinus reflex associated with aortic stenosis, or to the same mechanism that terminates life in patients suffering from anginal heart failure or recent myocardial infarction. The relationship between aortic stenosis and syncope is not clear in most instances, but the available evidence does not support the belief that fainting is due to cerebral anemia dependent upon inability of the left ventricle to force sufficient blood through the stenotic orifice. It is far more probable that loss of consciousness is due, in many instances at least, to hyperactivity of the carotid sinus reflex or to a reflex involving the same central and efferent pathways. The widespread impression that syncope is often a symptom of aortic insufficiency we believe to be erroneous.

From the standpoint of prognosis it is of some importance to realize that patients with aortic stenosis may die unexpectedly and with extreme suddenness. How frequently sudden death occurs in those subject to syncope cannot be stated on the basis of the present small group.

SUPPLEMENTARY NOTE

After this paper was written, Dr. Maurice Campbell of London was kind enough to send us full details of several of his cases, and with his consent two of them are briefly summarized herewith.

CASE 1.—A man of forty-six years had been well until January, 1930, when he complained of having to sit down frequently because of dizziness at his work. He had sometimes fainted but had not suffered from dyspnea. There was no substernal discomfort or pain, but a sensation as if the chest were fixed in position.

He had had rheumatism for five weeks in childhood. In August, 1929, his chest was squeezed against a truck when a heavy sack of grain fell upon him; he thought his ribs were fractured, but x-ray examination was negative.

Physical examination in April, 1930, showed the apex impulse of the heart to be one inch outside the mammary line. There was a coarse systolic murmur and thrill in the aortic area, and the aortic second sound was inaudible. No diastolic murmur was heard. Blood pressure was 140/70. There were no signs of congestive heart failure. Kahn and Wassermann reactions were negative.

Despite the advice of his attending physician, he insisted upon doing heavy physical work, and on the day of his death was engaged in digging a drain. When

bicycling home from work in December, 1931, he died suddenly. An autopsy was performed in a neighboring house; the essential finding was extreme stenosis of the aortic orifice, which was almost totally closed. There was marked calcification of the cusps. There was a healed tuberculous nodule at the apex of the left lung and a cystic left kidney; otherwise there was nothing of interest. (The photographs sent by Dr. Campbell show that the aortic orifice was just large enough to admit a small probe.)

CASE 2.—A woman of forty-two years who was admitted to the hospital on June 20, 1934, complained of breathlessness, fatigue and loss of weight. She had been subject to syncopal attacks for three years, and syncope preceded the usual symptoms of congestive heart failure. Her past history disclosed no illnesses of importance other than scarlet fever at the age of seventeen years.

At the time of admission she presented the usual signs of advanced congestive heart failure, but without ascites or hydrothorax. The heart was enlarged and presented a systolic thrill in the aortic area, and systolic and diastolic murmurs. There was gallop rhythm at the apex. The systolic blood pressure was 105; the diastolic indeterminate. The electrocardiogram showed normal sinus mechanism with left axis deviation. Orthodiagram showed enlargement of the left ventricle; the transverse diameter of the heart was 14.5 cm. and that of the thorax 22 cm.

The patient responded splendidly to the administration of digitalis and salyrgan. Just as she was about to start getting up, she died very suddenly in syncope. Postmortem examination showed the aortic valve reduced to a very small slit. The cusps were calcified and absolutely rigid. The mitral and tricuspid valves were normal, as were the coronary arteries. There was great hypertrophy of the left ventricle.

Dr. Campbell adds the comment that death in this case was absolutely sudden and unexpected, and that he believes it to be not uncommon in this type of aortic stenosis.

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FURTHER EXPERIENCES WITH TOTAL THYROIDECTOMY IN THE TREATMENT OF INTRACTABLE HEART DISEASE*

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SINCE it was first suggested[1] that the removal of a normal thyroid gland might be helpful in the treatment of intractable chronic heart disease, a sufficient time has elapsed to permit of at least a preliminary review of its value. This present analysis will be confined to cases which were treated at the Peter Bent Brigham Hospital. The first twelve such cases were previously reported,[2] and some follow-up notes of these will be discussed below. The main purpose is to report thirty additional cases in which the normal thyroid gland was completely removed and to evaluate the results obtained.

REVIEW OF CASES PREVIOUSLY REPORTED

In the first two cases a subtotal thyroidectomy was performed. When it was found[3] in some cases that clinical improvement was temporary, it was thought that the remaining tissue had regenerated, and therefore complete removal of the gland was practiced thereafter. These first twelve patients were suffering from far advanced cardiac disease. It seemed only justifiable to try out a new procedure in hopeless cases when life was practically intolerable. The therapeutic results must be viewed with this in mind.

CASE 1. (Med. No. 37679.) Female, sixty-one years old. Diagnosis: hypertensive heart disease, auricular fibrillation and extreme congestive failure. Operation: subtotal thyroidectomy June 27, 1927, by Dr. F. C. Newton. Patient made an extraordinary and unexpected improvement, remained ambulatory and in good health and free from all congestion for about four years. She died with congestive heart failure on January 16, 1932.

CASE 2. (Med. No. 40940.) Male, fifty-three years old. Diagnosis: hypertension and angina pectoris. Subtotal thyroidectomy was performed on June 15, 1932, by Dr. John Homans. The anginal attacks were slightly improved. He died of angina pectoris on January 12, 1934. The result here was not satisfactory.

CASE 3. (Med. No. 42478.) Male, forty-three years old. Diagnosis: thromboangiitis obliterans, hypertension with both congestive failure and angina pectoris, cirrhosis of liver (?), thrombosis of portal vein (?). Total thyroidectomy was performed December 14, 1932.† The anginal attacks disappeared entirely for about six months and were only rare thereafter. Dyspnea and recurrent ascites developed, the

*From the Medical and Surgical Clinics of the Peter Bent Brigham Hospital, Boston, Mass.

†This and all subsequent operations were performed by Dr. E. C. Cutler, surgeon-in-chief of the Peter Bent Brigham Hospital.

entire course being rather atypical. He died on September 7, 1932. Post-mortem examination showed thrombosis with almost complete occlusion of the abdominal aorta and extreme sclerosis with tendency to occlusion of almost all the arteries of the body. No thyroid tissue remained. The result in this case was excellent for angina pectoris during the nine months of his life.

CASE 4. (Med. No. 39768.) Female, sixty-one years old. Diagnosis: hypertension, severe angina pectoris, moderate congestive heart failure, and previous coronary thrombosis. Operation February 4, 1933. There was complete relief of angina for five months when a second attack of coronary thrombosis occurred. Since then angina has recurred infrequently. The element of dyspnea is slightly ameliorated. Fifteen months after the operation the result can be considered satisfactory.

CASE 5. (Med. No. 41570.) Male, sixty-one years old. Diagnosis: chronic myocarditis, complete heart-block, auricular fibrillation and marked congestive failure. Operation March 9, 1933. Improvement was marked. Patient remained ambulatory and comfortable for four months. Ascites then developed and he died August 27, 1933. Post-mortem examination showed fibrous myocarditis and cirrhosis of the liver. The result here, though of short duration, was excellent, for a bedridden cardiac patient requiring frequent chest taps was made comfortable and ambulatory for some months.

CASE 6. (Med. No. 40453.) Female, forty years old. Diagnosis: mitral and aortic stenosis and insufficiency, auricular fibrillation, calcification of pericardium and marked congestive failure. Operation April 7, 1933. This patient's life, which had been quite miserable for a few years so that she was in hospitals practically all the time, was slightly improved. She is still alive thirteen months after operation but is invalided.

CASE 7. (Med. No. 42742.) Male, seventy years old. Diagnosis: coronary thrombosis (recent), marked congestive failure. Operation April 11, 1933, while he was practically moribund. Died the following day. Post-mortem examination showed occlusion of the left coronary artery and aneurysm of the left ventricle. It was an error to have operated on such a patient.

CASE 8. (Med. No. 42822.) Male, fifty-three years old. Diagnosis: mitral stenosis, auricular fibrillation, marked congestive heart failure. Operation May 19, 1933. There was slight apparent improvement for a few months. He gradually failed and died on October 8, 1933. Post-mortem examination showed calcified stenosis of mitral and aortic valves. Three small bits of thyroid tissue were found, weighing about one gram.

CASE 9. (Med. No. 43101.) Male, forty-five years old. Diagnosis: mitral stenosis, auricular fibrillation, cirrhosis of liver. Operation May 26, 1933. Improvement was only very slight. He died September 22, 1933, two days after an exploratory pericardiotomy. Post-mortem examination showed marked mitral stenosis and "Zuckergussleber."

CASE 10. (Med. No. 42229.) Female, twenty-nine years old. Diagnosis: mitral stenosis, auricular fibrillation, chronic nephritis and marked congestive heart failure. Operation June 5, 1933. Improvement was very slight. She required several hospital readmissions, although she was able to lie flat—which was impossible before operation. She died on March 21, 1934.

CASE 11. (Med. No. 43259.) Male, fifty-nine years old. Diagnosis: syphilitic aortitis, aortic insufficiency, angina pectoris and cardiac asthma. Operation July 7, 1933. There was complete freedom from anginal attacks which previously were frequent and most severe. He died at home in an attack of acute pulmonary edema on July 26, 1933, after a few days of nocturnal dyspnea.

CASE 12. (Med. No. 43307.) Colored male, forty-three years old. Diagnosis: hypertensive heart disease, auricular fibrillation with marked congestive failure. Operation August 3, 1933. Now, ten months after operation the patient is ambulatory and leading a life of moderate activity. The improvement here seems extraordinary considering the grave, refractory preoperative condition.

In judging the value of the results obtained in the first twelve cases and also in those to be reported below, there are various considerations that need to be taken into account. In the first place, one must ascertain whether improvement took place either in the elements that make up the picture of congestive heart failure or in the frequency and severity of the anginal attacks. These are the two purposes for which the operation is intended. A second question which arises is whether any significant harmful effects resulted from the operation. Finally one might rightfully ask whether improvement, if it occurs, is worth while. The severity of the diseases with which these patients were suffering is clearly indicated by the fact that six of the nine patients who survived total thyroidectomy died of heart disease within nine months. The first two patients with subtotal thyroidectomy survived four and one-half and one and one-half years respectively. There were three who are still alive, sixteen, fourteen, and ten months after total thyroidectomy. One of these three is bedridden; although her life is probably prolonged, her impoverished economic state has made the survival period a great burden to her and to those caring for her. The careful analysis of the preoperative and postoperative events shows that some improvement, though occasionally only slight, took place in all instances. The advanced stage of the underlying pathological processes did not permit most of these patients to enjoy the improvement for any great length of time. The fact that any improvement could occur and that a few were rendered ambulatory after having been bedridden previously gave us courage to continue this work. In the following cases, however, an attempt was made to select somewhat more hopeful patients.

SELECTION OF CASES

In the selection of cases there are a few fundamental principles which, in the present stage of this work, are directly applicable. No patient should be subjected to this operation who is able to carry on his occupation. Furthermore, if the patient is unable to work, but his financial status permits him to lead a life of leisure, provided he is comfortable, operation would not be advised. It is obvious that the economic and social status of the individual plays an important rôle in selection. If a man has angina pectoris and either gets adequate relief by taking nitroglycerin or is able to lead a life which avoids attacks, he would not be considered a suitable case. On the other hand, if the same man had to do some walking which was necessary in his

daily work and he was dependent upon this for a livelihood, operation would be recommended with the hope of economic rehabilitation. There is as yet no evidence to show that the operation prolongs the life of a patient with angina pectoris, and therefore it cannot be recommended with this in view. In fact, as will be seen later, subsequent coronary thrombosis has not been prevented by total thyroidectomy. It follows, therefore, that in a patient with angina pectoris the specific criteria to help in the selection of suitable cases are the frequency and severity of attacks and to what extent they are making life intolerable. So far, the level of the blood pressure, the history of previous coronary thromboses or the presence of abnormalities in the electrocardiograms have not been significant factors in our selection. If the attack of coronary thrombosis was very recent, a sufficient time should have elapsed to permit one to judge whether recurrent anginal attacks will be troublesome or not.

With regard to selection of cases with congestive heart failure, the problem is more difficult. There are some obvious contraindications to the operation, i.e., bacterial endocarditis or active rheumatic carditis. It is not known that infections of any sort would be materially helped by this procedure. A further contraindication is an accompanying renal insufficiency not dependent upon simple passive congestion of the kidneys. Likewise cirrhosis of the liver presents a real handicap. It may be difficult to ascertain whether an enlarged liver in the presence of congestion is irreparably cirrhotic or will recede with improvement in the circulation. The frequency of repeated abdominal tappings and the length of time which the liver has been known to be enlarged, help somewhat in differentiating the two conditions. Furthermore it might be inadvisable to select a patient who has some unrelated handicap like hemiplegia which would of itself greatly diminish the value of any improvement that the operation might produce. Finally, the ordinary life expectancy, the history or pattern of the particular cardiac disease needs careful consideration. It is well known that when significant congestive heart failure develops in patients with aortic stenosis or luetic aortic insufficiency the expected span of life is very short. Only a more extensive experience will tell whether such patients may be expected to receive consistent improvement by the operation. At present if such patients are selected at all, it should be done with no great optimism.

Mitral stenosis and hypertension associated with congestive failure are more liable to go through several cycles of relapses and remissions extending over a longer time and from this point of view are more suitable. Auricular fibrillation which is present in the more advanced stages of mitral stenosis instead of making patients less suitable for operation, seems to have made them more so. This is particularly true if the ventricular rate with auricular fibrillation does not slow satis-

factorily on full doses of digitalis, for we have found that such slowing occurs more readily after operation. The close association of auricular fibrillation with hyperthyroidism and the experimental production of auricular fibrillation in experimental hyperthyroid animals by the injection of adrenalin[4] make one suspect that there may be some relationship between the normal thyroid gland and this arrhythmia.

In all this work, the so-called accidents of heart disease, like pulmonary infarction, peripheral emboli, coronary thrombosis, and hemiplegia, will inevitably occur in one case or another entirely unexpectedly whether operation is performed or not. We have had patients die suddenly a few days before the day set for the operation as well as after the operation. Such distressing possible complications must not be regarded very seriously in estimating the value of the operation or in the selection of cases unless they occur with undue frequency directly after the operation.

Finally in considering congestive heart failure there are two aspects that need clear differentiation, i.e., the subjective and objective evidences of circulatory insufficiency. The subjective symptoms, palpitation and especially breathlessness, frequently precede, by some years, the objective findings of peripheral edema, engorged liver, or moisture in the lungs. The difficulty in interpretation of the subjective complaints is very great because these same symptoms are present without organic heart disease and even when found in patients with obvious valvular disease need be related in no way to circulatory insufficiency. In other words, dyspnea, palpitation, and weakness may occur for many years in cases of well-compensated organic cardiac disease and in some cases will give a false estimate of the duration of congestive failure. The objective criteria, on the other hand, are readily determined and will serve as more reliable guides as to the presence or absence of congestive failure.

The following cases to be reported were more carefully selected. On the whole, the morbid processes were not regarded as so severe as in the first group, but the same criteria discussed above were followed. All the patients were incapacitated and unable to work. All those suffering from angina pectoris had attacks at rest as well as on effort. All those with congestive heart failure gave very little promise of ever being comfortable while ambulatory.

INTERPRETATION OF IMPROVEMENT

The matter of interpreting the results and indicating the degree of improvement is a difficult one. In angina pectoris the disability is very much a subjective one and depends on a variety of different circumstances, such as emotional factors, food intake, temperature changes, and the like. The number of nitroglycerin pills is some guide but not necessarily an accurate one, for the patient may remain suffi-

ciently inactive to avoid attacks. The best single guide is the ability to walk out of doors. Inasmuch as a good many of our patients were operated upon in the fall, their ability or inability to walk during the succeeding unusually cold winter was as severe a functional test as one might have. The results were regarded as excellent if there were no attacks or practically no attacks following operation with the patient ambulatory. Whether they returned to work or not could not be used as a measure of success, because some could find no occupation and others were retired. There are other instances in which they were advised not to resume an active occupation because it seemed wise under the circumstances to rest content with a comparative freedom from attacks. Numerically the term "excellent" might be regarded as 75 to 100 per cent improvement. The result was "good" when the improvement could be estimated as 50 to 75 per cent, "moderately good" as 25 to 50 per cent and "fair" if the amelioration was less than this. Even in the best instances belonging to the excellent group, attacks could recur under unusual circumstances. The same general terminology was used in cases of congestive heart failure, and here again the criteria were somewhat arbitrary and open to personal judgment. If the condition was far advanced and the patient bedridden, the result can be regarded as excellent if the patient is rendered comfortable and ambulatory although he never is able to work. One really has to compare the result obtained with the expectations under usual methods of treatment.

RÉSUMÉ OF CASES OF ANGINA PECTORIS AND CLINICAL RESULTS OF THE OPERATION

This report contains 23 cases* of angina pectoris in which a complete extirpation of a normal thyroid gland was performed. (Table I.) There were 14 males and 9 females. The average age of the males was 60.1 years, the extremes being 42 and 72 years. The average age of the females was 61.7 years, the extremes being 52 and 67 years. The duration of angina pectoris at the time of the operation was 4.6 years for the males and 5.1 years for the females. This series is, of course, rather small, but so far as the figures go the patients here have already lived the average length of life following the onset of angina. In a recent study of 141 fatal cases of angina pectoris[5] it was found that the average length of life after the onset of angina was 4.6 years for the males and 4.5 years for the females. It follows from this that the average life expectancy in the group operated upon is not great. Although nothing is known about the effect of total thyroidectomy on the duration of life in angina, future history of such cases will throw much light on this question. The primary purpose of the procedure

*Case summaries will be published with the reprints.

TABLE

CASE	AGE	SEX	DATE OF OPERATION	DIAGNOSIS	SYMPTOMS
13	60	F.	8/22/33	Angina	8 yr. duration. 2-5 attacks daily.
14	58	M.	9/21/33	Angina	3 yr. duration. 5 attacks daily. Coronary thrombosis 1931-1932.
15	55	M.	9/22/33	Angina	2 yr. duration. 1-300 attacks per week.
16	64	M.	9/22/33	Angina, diabetes, and gallstones	3 yr. duration. Coronary thrombosis. 1931 1-2 attacks daily.
17	42	M.	10/17/33	Angina	12 yr. duration. 100 attacks weekly.
18	60	F.	10/25/33	Angina	1 yr. duration. Coronary thrombosis 1933. Moderate frequency, each 15-30 min.
19	52	F.	10/26/33	Angina, hypertension, and heart failure	4 yr. duration. Nocturnal dyspnea several months. Coronary thrombosis 1931-1933.
20	61	M.	10/28/33	Angina	2 yr. duration. Attacks of moderate frequency.
21	63	M.	10/28/33	Angina and diabetes	3½ yr. duration. Attacks of great severity. 6-10 daily. Coronary thrombosis. June, 1933.
22	61	F.	11/ 1/33	Angina	5 yr. duration. Moderate severity and frequency. Coronary thrombosis 1928.
23	65	F.	11/ 2/33	Angina	10 yr. duration. 10-15 attacks daily.
24	66	M.	11/13/33	Angina	9 yr. duration. 5-10 attacks daily.
25	67	M.	11/22/33	Angina and diabetes	1 yr. duration. Attacks severe and 1 daily.
26	65	F.	11/29/33	Angina	7 mo. duration. Attacks quite severe and very frequent.
27	53	M.	12/ 7/33	Angina	6½ yr. duration. 10 attacks daily. Coronary thrombosis 1932.

*This patient never developed sufficient myxedema to require treatment.

I

BASAL METABOLISM			BLOOD PRESSURE	RESULT	COMMENT
PRE-OPERATIVE	MYXEDEMA	ON THYROID THERAPY			
+12%	−30%	−15%	200/100	Excellent	Only 2 attacks in 10 months. Doing all housework.
− 8	−19	−14	145/80	Excellent	Only rare attacks on severe exertion—8 months.
+ 4	−15	−11	138/86	Excellent	No attacks for 9 months.
+ 8	−24	−	120/54	Moderately good	Much fewer attacks in past 8 months.
−14	−33	−21	130/80	Moderately good	Attacks milder and about ½ as frequent—8 months.
− 3	−28	−14	182/100	Good	Attacks much milder and infrequent—8 months.
+ 8	− 7*	−	140/110	Fair	Attacks much less troublesome but dyspnea persists—8 months.
− 5	−27	−24	120/90	Excellent	For 8 months can walk freely.
− 5	−13	−19	146/92	Fair	For 8 months attacks less severe and less frequent.
− 7	−36	−11	140/70	Excellent	Returned to work, but May, 1934, developed some congestive failure; no angina.
− 9	−28	−22	190/90	Moderately good	For 8 months no attacks at rest, but recur on moderate exertion.
− 6	−22	−27	175/90	Moderately good	Returned to work and for 7 months attacks have been much milder and less frequent.
− 5	−	−	140/80	Died 5 days postoperative	No attacks for 5 days postoperative. Out of bed feeling fine, then had fatal coronary thrombosis.
−11	−24	−25	220/110	Good	For 7 months attacks rare—very mild and none at rest.
−18	−32	−24	110/68	Excellent to fair	For 6 weeks no attacks, then they recurred before thyroid extract was started. 4 months postoperative fatal acute coronary thrombosis.

TABLE I

CASE	AGE	SEX	DATE OF OPERATION	DIAGNOSIS	SYMPTOMS
28	61	M.	12/ 8/33	Angina, transient auricular flutter	7 yr. duration. Attacks very severe—4 daily.
29	67	F.	12/13/33	Angina	12 yr. duration. Attacks very severe and 5-6 daily.
30	65	M.	12/13/33	Angina	1 yr. duration. 6-7 attacks daily.
31	62	F.	1/ 4/34	Angina	15 mo. duration. Attacks very severe and frequent. Nitroglycerin ineffective.
32	54	M.	1/17/34	Angina	9 yr. duration. 2 attacks daily.
33	64	F.	1/20/34	Angina	3 yr. duration. Attacks of moderate severity and frequency.
34	56	M.	3/ 5/34	Angina and myocardial failure	4 yr. duration. Coronary thrombosis. 1931. Attacks moderate frequency and severity.
35	72	M.	3/ 6/34	Angina and paralysis agitans	9 mo. duration. Attacks 2-3 daily. Very severe. Nitroglycerin ineffective.
36	33	M.	10/16/33	Mitral stenosis, aortic insufficiency, and auricular fibrillation	Dyspnea 5 months. Progressively worse, finally marked failure.
37	54	M.	12/ 6/33	Mitral stenosis, auricular fibrillation, emphysema, and duodenal ulcer	Dyspnea 3 yr. Marked decompensation 1 week.
38	40	M.	1/13/34	Mitral stenosis, depressive psychosis	Increasing dyspnea 4 yr. Attacks acute pulmonary edema. Psychosis.
39	39	F.	1/27/34	Mitral stenosis, auricular fibrillation	Dyspnea 7 yr. Frequent decompensation.
40	50	M.	2/ 8/34	Chronic myocarditis, auricular fibrillation, emphysema	4 attacks of decompensation in 11 yr.
41	44	M.	2/12/34	Mitral stenosis, aortic insufficiency, auricular fibrillation	7 yr. increasing dyspnea.
42	30	F.	2/13/34	Mitral stenosis, aortic insufficiency	3 yr. increasing dyspnea. In bed 3 months.

—CONT'D

BASAL METABOLISM			BLOOD PRESSURE	RESULT	COMMENT
PRE-OPERATIVE	MYXEDEMA	ON THYROID THERAPY			
+ 8	–29	– 5	160/110	Excellent	No attacks for six months.
– 9	–	–	150/90	Died 1 day post-operative	Patient begged for relief. Attacks unbearable. Fatal acute coronary thrombosis 1 day postoperatively.
+ 1	– 9	0	178/100	Good	Only occasional attacks for 6 months mainly because he is more active.
– 4	–	–	180/110	Died 1 day post-operative	Fatal acute pulmonary complication 1 day postoperatively.
– 3	–21	–	134/80	Good	Attacks only on severe exertion 6 months.
+15	+ 3	+ 3	218/100	Good	Attacks on moderate exertion 4 months.
– 4	–28	–23	130/85	Excellent	No attacks. Walking freely 3 months.
+ 7	–20	–	160/80	Excellent	No attacks 3 months.
– 1	–31	–21	140/90	Excellent	Ambulatory. Working. Symptom-free 8 months.
– 6	–22	–36	140/80	Good	Ambulatory. Comfortable 5 months. One slight break in compensation.
+22	–	–	120/80	Failure	Died Feb. 16, 1934. Mesenteric thrombosis, acute pulmonary edema.
+16	–21	– 7	125/90	Excellent	Does housework without symptoms—6 months.
+21	–21	–15	130/90	Fair	Subjective improvement. Ambulatory.
– 9	–30	–18	120/96	Excellent	4 months ambulatory. Working.
+15	–19	–16	122/64	Good	4 months ambulatory. Dyspnea on moderate exertion.

was relief of anginal pain, for it is already known that subsequent coronary thrombosis is not prevented by total thyroidectomy.

The clinical results in the relief of anginal pain were divided into four gradations according to the method explained above: excellent, good, moderately good, and fair. Among these 23 patients there were 2 which were regarded as postoperative deaths. Another patient died five days after operation of typical coronary thrombosis, having been entirely free from pain during the interval, and a fourth who had an excellent result for six weeks followed by a recurrence of anginal pain of moderate degree, finally died four months after the operation of acute coronary thrombosis. Of the remaining 19 who are all still alive, the results were "excellent" 8, "good" 6, "moderately good" 4, and "fair" 1. In three of these there were varying degrees of congestive heart failure in addition to angina pectoris, of which two have remained free of these symptoms and one has had increasing myocardial failure. The average duration of follow-up observation on the 19 living patients is six months, the longest is over ten months, and the shortest over three months.* Considering the fact that these patients were selected only because their symptoms were refractory to the ordinary methods available, that the attacks came at rest as well as on effort, and that the attacks were sufficiently crippling to make life hardly worth while, it is fair to consider that the results were quite satisfactory.

Observation on the Basal Metabolic Rate

The preoperative basal metabolic rates in these cases varied a good deal. The average was +1 per cent. The extremes were –18 per cent and +15 per cent. We have learned from experience of the past two years that there are occasional individuals showing basal metabolic rate of +20 per cent to +45 per cent, with no clinical signs of hyperthyroidism, in whom the thyroid gland is normal on gross and microscopic examination. Such cases have been found in which the high rate could not be accounted for by dyspnea or psychic influences. This occasionally may lead to confusion in preoperative diagnosis, as at times it has been impossible to predict whether we were dealing with a case of masked hyperthyroidism or a cardiac with a normal thyroid gland.

The speed with which the basal metabolic rate fell after operation was not constant. Thyroid gland was administered to these patients when they first began to complain of symptoms pointing to myxedema. The average metabolic rate at this point was –23 per cent. There

*Since this paper was submitted, three of the patients have died: one (Case 16), one day after cholecystectomy, of coronary thrombosis; and two others (Cases 23 and 33), of coronary thrombosis. The intervals after thyroidectomy were ten, sixteen, and twelve months, respectively. All those with congestive heart failure are still living. The follow-up period is now nine months longer than the time mentioned in the text.

were other evidences of the hypothyroid state before this point was reached, such as a pallor or a change of facial expression and hypercholesterinemia. But if the time at which it seemed advisable to administer thyroid gland is taken as an index, the average interval after operation was found to be 65.4 days; the longest was 94 days and the shortest 38 days. The average metabolic rate after thyroid extract was administered was –16 per cent. At first glance one might expect that those with a lower preoperative basal metabolic rate would develop myxedema more rapidly than those with a high rate. No significant difference was found, however, in this study. The average time of the former group with an average basal metabolic rate of –8 per cent was 64.2 days and of the latter with an average basal metabolic rate of +10 per cent was 67.1 days. It is of some interest that in occasional instances the basal metabolic rate had fallen but very little even one to two months after the operation. One patient with a preoperative reading of +15 per cent had a basal metabolic rate of +3 per cent 48 days after total thyroidectomy. At this time there were some clinical evidences of myxedema such as dryness of the skin and somnolence and the blood cholesterol had risen to 610 mg. per cent. The administration of thyroid gland was begun at this point despite the absence of a low metabolic rate. Another patient showed a similar course. These variations in the fall of the metabolic rate are probably dependent upon variations in the speed in which the remaining thyroid substances disappear from the body and on variations in the balance of the other endocrine glands. In none of the cases was the metabolic rate allowed to reach the very low levels seen in spontaneous myxedema. Attention has recently been called by Means and Lerman[6] to the variations in the time at which different aspects of the hypothyroid state may be expected to develop after the function of the thyroid gland has been impaired. It is likely that the so-called "myxedematous heart" requires years for its development, and the same may be true of secondary anemia. Whether such ultimate changes will occur in these patients in whom the very low levels of metabolism are prevented by the feeding of thyroid extract is problematic though unlikely. In general, an attempt was made to keep the metabolic level of these cases around –20 per cent.

Velocity of Blood Flow

Measurements of the velocity of blood flow in patients with angina pectoris operated upon can reflect fairly clearly the effect of artificial myxedema on the speed of circulation. In these the element of congestive heart failure with its accompanied slowing of the circulation does not necessarily exist. The average preoperative rate of blood flow measured by the sodium cyanide method[7] in these 23 cases was 20 seconds (average basal metabolic rate +1 per cent). Four days

after the operation when the average basal metabolic rate was –1 per cent the average circulation time was still 20 seconds. When symptoms of myxedema were sufficient to warrant treatment (65 days postoperative), the average basal metabolic rate was –25 per cent and the circulation time was 32 seconds, i.e., approximately a fall of ½ second for each 1 per cent drop in the metabolic rate. The approximation is in accord with the readings obtained in a group of patients after the administration of thyroid gland. As the basal metabolic rate rose to an average level of –14 per cent the speed of circulation increased to an average of 26 seconds. Unlike the observations to be discussed below in cases of congestive heart failure, every case of angina showed consistent slowing of the speed of circulation after operation as the basal metabolic rate fell. This is in accord with the findings of Blumgart and his coworkers[8] in spontaneous myxedemas.

Changes in Blood Cholesterol

Determinations of the cholesterol content of the blood were made on 11 cases of angina pectoris. The method of Bloor was used; and although the control figures seemed higher than those given for normal individuals, the changes detected were sufficiently great to be of distinct significance. The average finding before operation in this series was 244 mg. per cent. The high normal figure may be due to the age of these patients, or it may be related to the fact that they all had vascular disease. The second determination was made about five days after the operation, and the average was found to be 260 mg. per cent. At the point of clinical myxedema this figure had risen to 488 mg. per cent and then subsequently fell to an average of 329 mg. per cent as a result of the administration of thyroid extract. In practically all instances, the cholesterol content of the blood is continuing at a higher level than before operation. This is apparently a necessary result of our attempt at keeping the metabolic rate around –20 per cent. These findings are in general in accord with those published by Mason, Hunt and Hurxthal[9] in spontaneous myxedema. Whatever ultimate deleterious effect this hypercholesterinemia may have, will become apparent only in the future study of these cases.

Changes in the Size of the Heart

Careful measurements of the size of the heart as determined by roentgenograms taken at a distance of seven feet were made in ten of the patients with angina pectoris. The distance of the right and left borders from the midline (Mr. and Ml.), the diameter of the aortic shadow (G.V.), the internal diameter of the chest (I.D.) and the transverse diameter of the heart (T.D.) were charted. The average preoperative figures when the basal metabolic rate was +1 per cent were Mr. 4.4 cm., Ml. 9.4 cm., G.V. 5.7 cm., I.D. 28.7 cm., and T.D. 13.8 cm.

About two months after operation when symptoms of myxedema were present (basal metabolic rate –26 per cent), the corresponding average figures were Mr. 4 8 cm., Ml. 10 0 cm., G.V. 6.0 cm., I.D. 29.2 cm., and T.D. 14.8 cm. From these figures it seems that the average transverse diameter of the heart increased by 1 cm. This increase occurred both on the right and on the left side of the heart about equally. The increase in the size of the aortic shadow was only 0.3 cm. and may be within the limit of error. Further observations were made about two months later after the basal metabolic rate had been raised to an average level of –12 per cent. Average measurements at this time were as follows: Mr. 4.8 cm., Ml. 10.4 cm., G.V. 6.1 cm., I.D. 29.1 cm., and T.D. 15.2 cm. The transverse diameter of the heart at the time these last measurements were taken on the average of 141 days after the operation, showed a very slight further increase. The figure was then 1.4 cm. greater than that of the preoperative diameter. The slight increase continued despite the rise in the basal metabolic rate brought about by thyroid extract. These changes cannot be regarded as insignificant despite the fact that the average internal diameter of the chest also increased 0.4 cm. over the preoperative level. It can be regarded either that this latter increase was within the error of measurement or that the chest was held in a more expanded condition after than before operation. One is led to suspect that a slow, steady dilatation is taking place in these patients as a result of prolonged, mild myxedema which is not entirely compensated for by the small doses of thyroid extract.

Observation on the Blood Pressure

The preoperative level of the blood pressure in these 23 patients with angina pectoris varied a great deal. There were some with hypotension and others with marked hypertension. The average pressure was systolic 152 mm. and diastolic 90 mm. The extremes for the systolic pressure were 120 mm. and 225 mm., and for the diastolic 68 mm. and 150 mm. About one week after the operation the average systolic was about 141 mm. and diastolic 82 mm. The fall in the level of blood pressure can be ascribed either to the continued rest in bed or as a result of the removal of the thyroid gland. It cannot be due to a fall in the metabolic rate for this had not as yet occurred. About two months after the operation when symptoms of clinical myxedema were present, the average systolic pressure was 167 mm. and the average diastolic was 96 mm. The patients were now ambulatory, and the slight rise over the preoperative level can easily be explained on this basis. After a period of almost six months had elapsed following the operation, the average readings were systolic 163 mm. and diastolic 93 mm. In general it can be said that although there may be a slight tendency for the blood pressure to rise, no significant variations have been detected over an average period of six months.

Changes in Weight

It is well known that with the hypothyroid state there is a tendency to gain weight. This proved to be true in these cases of angina pectoris. The average preoperative weight of 11 patients was 67.4 kg. About two months later when they had clinical evidence of myxedema, the average weight was 72.0 kg. Six months after operation, although they had all been taking small doses of thyroid extract so that the basal metabolic rate had increased somewhat from the previous low level, the average weight was 73.2 kg. Inasmuch as none of these patients had congestive heart failure, the gain of almost 6 kg. in six months cannot be ascribed to the type of water retention that accompanies congestive failure. It must be interpreted as a direct result of the maintained lowering of the basal metabolism. Furthermore the increase in weight was not retarded by the small doses of the thyroid extract which it seemed desirable for them to take.

Possibility of Secondary Anemia

One of the recognized accompaniments of spontaneous myxedema is a secondary anemia.[10] Although it is more likely that this sort of anemia develops only after the myxedema has continued for some years, it is naturally of interest to know whether blood changes of this type developed in our cases in which artificial myxedema was produced. Careful estimates of the hemoglobin and erythrocyte counts were made in eleven cases. The preoperative figures for these two determinations were respectively 85 per cent and 4.8 millions. At an average interval of 96 days after operation the corresponding figures were 87 per cent and 4.7 millions. It is evident that during this brief period anemia had not developed. In a few instances examinations as long as nine months after operation failed to show any development of anemia. It would not be surprising if this did occur in some of these patients after a lapse of years.

Observations on the Vital Capacity of the Lungs

There is nothing inherent in the mechanism of angina pectoris which diminishes the vital capacity of the lungs. When the vital capacity in this condition is compared to the customary normal standards, it has been found to be somewhat diminished,[11] primarily because a fall is to be expected normally with advancing years. Furthermore in myxedema unaccompanied by congestive heart failure, dyspnea is not an integral symptom and the vital capacity is therefore unchanged. Observations on this series of cases confirm the above impressions. The average preoperative vital capacity of 18 patients was 2,630 c.c. About one week after operation the figure was 2,590 c.c., two months later when clinical evidence of myxedema was present it was 2,670 c.c., and

about two months after this following the administration of thyroid extract it was 2,600 c.c. In a word, the vital capacity of the lungs remained unchanged in cases of angina pectoris following thyroidectomy.

Changes in the Electrocardiograms

Frequent reference has been made to changes in the electrocardiogram which characterize spontaneous myxedema. Essentially they consist in a diminution of all electrical complexes both auricular and ventricular with particular flattening of the T-waves. Like many other bodily changes which result from myxedema, these alterations probably require years for their production. During the comparatively short period that the patients in this study have been observed, no such marked findings have been noted. In some there was slight but distinct lowering of the amplitude of the QRS complex and the T-waves. In a few the P-wave was also diminished. Occasionally no significant changes were detected. It is likely that because these patients are not permitted to remain in a state of marked myxedema, the characteristic electrocardiographic evidences of "myxedema heart" did not supervene.

RÉSUMÉ OF PATIENTS WITH CONGESTIVE HEART FAILURE AND CLINICAL RESULTS OF THE OPERATION

In the second series of cases reported here there were seven cases* of congestive heart failure, five males and two females. The average age of the former was 44 years and of the latter 35 years. Six had mitral stenosis, of which four had auricular fibrillation and two had a regular rhythm (one of the latter had paroxysmal auricular flutter). Three of these valvular cases had additional involvement of the aortic valve with aortic regurgitation. There was one nonvalvular case in which there were myocardial failure and auricular fibrillation associated with a previous hypertension. The average duration of symptoms which we regarded as evidences of congestive heart failure was 4.8 years. This figure would have been shorter except for one patient who had a history going back for eleven years. The duration of objective evidence of congestive heart failure must have been distinctly less than 4.8 years, but it is impossible to determine this figure exactly. We estimated the improvement as excellent in three of these cases (No. 36, 39 and 41), good in two (No. 37 and 42), fair in one (No. 40), and as absent in one (No. 38). The three regarded as excellent have remained free from objective and subjective evidences of circulatory failure while ambulatory for intervals of eight months, six months, and four months. The others have had varying degrees of improvement. In the one case classified as a failure the patient died five weeks after operation of acute pulmonary edema following a mesenteric thrombosis. Even this patient, judged by his ability to breathe, had improved

*Case summaries will be published with the reprints.

shortly after operation. The one that seems to have had the least benefit was the nonvalvular patient with a history of dyspnea of eleven years' duration. Although recurrent edema and some ascites have developed, the factor of breathlessness has improved; for, whereas before operation he was orthopneic, he can now lie flat.

A general survey of the cases of congestive heart failure and those reported in the first series confirms our earlier impression that complete thyroidectomy is not so helpful in this condition as it is in angina pectoris. To be sure, it is not a simple matter to judge the result of treatment and the progress of congestive failure, because factors like intercurrent infection, infarction, and other so-called unexpected accidents of heart disease, may suddenly change the clinical picture. Furthermore, the inherent progress of the disease varies so much in speed that in some cases it may quickly overtake the benefits derived from the operation. At the present time, the exact factors that determine the choice of patients with congestive heart failure are not clear. Although one prefers those cases that become free of objective evidence of failure on the preoperative medical care, we have had several instances in which the liver was still markedly enlarged and recurrent hydrothorax was still present, only to see these entirely disappear within ten days after operation.

The average preoperative basal metabolic rate in these seven cases was +8 per cent; they varied from –9 per cent to +22 per cent. The average rate when thyroid extract was first administered for myxedema was –24 per cent (an average of 68 days after operation). About ten weeks later, on thyroid medication the basal metabolic rate was –18 per cent. Although the desirable level varies somewhat with different patients, this last figure is approximately the optimum.

It has been shown that the velocity of blood flow is slowed in congestive heart failure and accelerates with improvement of the state of the circulation.[12] The last preoperative reading of these cases showed an average of 31 seconds. The basal metabolic rate at the time these readings were taken was +7 per cent. About two months later the basal rate was –26 per cent. The average circulation time was 40 seconds. This indicated an average slowing of the circulation of 9 seconds, accompanying a fall in metabolism of 33 per cent. The degree of slowing here was only half as great per unit fall in metabolism as that which occurred in patients with angina pectoris but without congestion. It is very significant that the patient (Case No. 36) who showed one of the most striking instances of improvement following operation was the only one who actually had an increase in the speed of circulation. The circulation time fell from 41 to 20 seconds as the metabolism fell from –4 per cent to –31 per cent. It is perfectly clear that unlike the anginal group, changes in the velocity of blood

flow in congestive heart failure subsequent to complete thyroidectomy are by no means constant. Similar inconsistencies between the basal metabolic rate and the velocity of blood flow are apparent on careful examination of the charts published by Blumgart and his coworkers.[13] One is quickly impressed by the fact that the degree of slowing of the circulation depends in a large measure upon the rate of blood flow before operation. When this rate is normal as in angina pectoris, a very consistent slowing occurs. Such slowing also results in some patients who have congestive heart failure but in whom the rate is approximately normal before operation. When the preoperative circulation time is considerably prolonged, however, if further slowing occurs it is only slight and there may be essentially no change or the rate may increase. The whole matter of the velocity of blood flow, although one factor in circulatory dynamics, is difficult of interpretation for it is so intricately dependent upon the total blood volume which shows considerable alterations during congestive failure.

It has long been known that the vital capacity of the lungs is diminished in congestive heart failure and increases as compensation improves. In these seven patients the preoperative vital capacity of the lungs was diminished, for the average was 2,100 c.c. At the point when clinical myxedema first was present, the reading was 2,190 c.c., and this rose slightly in a few months to 2,260 c.c., following the administration of thyroid extract. In two of these cases there was an increase of 600 c.c. or more following the operation, but on the whole one can say that the average change was very slight despite the fact that there was a decided improvement in the element of subjective dyspnea. In other words this method of treatment enabled the patient to breathe more comfortably, although the actual breathing space was essentially unaltered. The reason for this is probably that the needs for oxygen have been diminished and that the sensitivity of the nervous system was altered.

The changes in the size of the heart which took place in these cases, as measured by roentgenograms, were inconstant. The average transverse diameter before operation was 17.1 cm. when the basal metabolic rate was +3 per cent. Eighty-five days later when the average basal metabolic rate was –21 per cent, the transverse diameter was also 17.1 cm. Seventy-four days later when the average metabolism had risen to –16 per cent, as a result of the administration of thyroid extract the transverse diameter was 17.2 cm. In one case (No. 36) the heart size diminished 2.4 cm. and in another (No. 42) increased 1.2 cm. at the time of clinical myxedema. In contrast to patients with angina pectoris this group showed no consistent enlargement of the heart as the state of moderate myxedema continued. One may infer from this that with the improvement that takes place following thyroidectomy in cases of congestive heart failure there is a

tendency to diminution in the size of the heart which offsets the dilatation which would otherwise occur from myxedema.

The average preoperative blood pressure was 113 mm. systolic and 73 mm. diastolic. When the patients first had clinical evidences of myxedema the readings were 128 mm. systolic and 84 mm. diastolic, and at an average period of about five months later the blood pressure was essentially the same—129 mm. systolic and 78 mm. diastolic.

RATIONALE OF TOTAL THYROIDECTOMY AND DISCUSSION

For some years it has been apparent to many clinicians that the lowering of the basal metabolism exercises a beneficial effect on an embarrassed circulation. This has been true whether the circulatory failure was of the congestive or of the anginal type. The most outspoken evidence of this effect was witnessed in the extraordinary improvement that followed subtotal thyroidectomy in those patients with exophthalmic goiter or toxic adenoma who also showed gross cardiac disability. In fact, a considerable improvement was generally apparent concomitant with the fall of the basal metabolism that followed the administration of Lugol's solution, even before subtotal thyroidectomy. From a diametrically opposite direction there has been considerable clinical experience that also leads to the same conviction, i.e., that the state of the thyroid gland and the basal metabolism have a profound effect on the heart. It was frequently observed that cases with myxedema might easily develop angina pectoris or congestive failure as the metabolism would rise on thyroid administration.[14, 15, 16] The first instance of this we recall seeing was in 1925 when in a patient with myxedema the number of attacks of angina could be controlled entirely by the amount of thyroid he was given. When the metabolism was allowed to remain around –37 per cent, there were no attacks but there were symptoms of myxedema; and when it was –5 per cent there were frequent anginal attacks, with no clinical evidence of myxedema. It was found in this case that –15 per cent was about the optimum level. This relationship was currently known by many physicians who were specially interested in either thyroid or heart disease. Christian[15] in fact epitomized the situation in the statement that "thyroid deficiency may be a conservative process, a form of cardiac rest, that is advantageous to the heart."

Simultaneously considerable attention was also being paid to that small but fortunate group of cardiac cripples who had masked or latent hyperthyroidism. Here were patients suffering from advanced disabling heart disease who formerly succumbed because, although they had active hyperthyroidism, evidence of this was so obscure that it remained entirely overlooked. When such cases were properly diagnosed and the patients properly treated, it was found that many could be restored to very useful lives. This comparatively small group with

masked hyperthyroidism interested us intensely at the Peter Bent Brigham Hospital and formed the material for a series of clinical studies[1, 17, 18] which emphasized the importance and discussed the methods of arriving at the correct diagnosis.

Amid this enthusiastic search for masked hyperthyroidism among patients suffering from organic heart disease one patient was subjected to subtotal thyroidectomy in 1927 in whom the gland proved to be normal both in gross and in microscopic examination. Despite this a most extraordinary improvement followed which had not been obtained by all the customary measures employed before in this case. This fortuitous experience led to the inference that subtotal thyroidectomy of a normal gland might be helpful in the treatment of intractable heart failure. As time went on and this patient continued to be free from congestion, it seemed to warrant a conclusion then drawn that "the occurrence of striking improvement following subtotal thyroidectomy in a patient with advanced congestive failure, in whom the thyroid gland was normal, suggests that this operation may be useful more generally in the treatment of various forms of cardiac disease."[1]

Following this, deliberate removal of the thyroid gland was undertaken both at the Beth Israel Hospital and at the Peter Bent Brigham Hospital, in cardiac cases that were not responding to the routine methods of treatment. When it was found that in some of the cases in which a subtotal thyroidectomy was performed, clinical improvement and the simultaneous fall in the basal metabolic rate were only temporary, it was assumed that the remaining part of the gland could either regenerate or increase its activity.[3] The operation which was adopted for subsequent work therefore was a total thyroidectomy, the first one of which (Case 3, first series) was performed at the Peter Bent Brigham Hospital by Dr. E. C. Cutler, December 14, 1932. That such regeneration does not always occur after a subtotal thyroidectomy is illustrated by Case 4 of reference 3. Here, after nine-tenths of the gland was removed not only did the angina pectoris disappear but myxedema supervened, which has required constant thyroid medication for the past sixteen months.

Physiological studies on the circulation in heart failure and in disease of the thyroid gland were available to lend some support to the validity of this method of treatment. Particularly was this true of the observation on the velocity of blood flow by Blumgart and his associates.[8] It was found that congestive heart failure was accompanied by a slowing of the rate of blood flow and that with improvement the rate of blood flow accelerated. It was also found that in myxedema the rate of blood flow was slow in the absence of congestive failure. The conclusion that may be drawn from these observations is that with

a lowered metabolism the slow speed of the blood is adequate, and whether heart failure results in any case is a question of demand and supply, of the basal metabolic needs on the one hand and the rate of blood flow on the other. The therapeutic inference from this is that, when congestive failure is present, removing the thyroid gland may diminish the demand on the heart so that with a lowered metabolism the slow circulation will be adequate and compensation will be restored.

In this discussion it was hinted that the velocity of blood flow is a measure of the work of the heart. It may be an indirect index but hardly can be regarded as the accurate guide of the work of the heart. Better criteria would have been the volume output, the pressure relations, and rate at which the heart beats. Furthermore the prevailing conceptions concerning the mechanism of heart failure have been conflicting. The most recent work of Harrison and his associates[19] has shown that improvement in heart failure is independent of volume output of the heart. The latter may increase, decrease, or remain the same, the essential change being an improvement in the back pressure factor, i.e., diminution of venous or pulmonary engorgement. In fact they found that improvement in one case following total thyroidectomy was accompanied by a diminution in volume output of the heart. This is not in accord with the theoretical consideration of Blumgart and his coworkers[13] who stated that "if the normal metabolic rate of the patient with congestive failure were reduced, his blood supply while not necessarily altered, might nevertheless be sufficient for the lowered needs of the body."

Although one might offer the above explanation for the possible benefits to be derived from thyroidectomy in congestive heart failure, there is a distinct fallacy in these predictions. If in myxedema the rate of blood flow is slowed as a result of the lowered metabolism, would one not have to postulate that when myxedema is produced surgically for congestive heart failure, which already has a slow circulation, the speed of blood flow would be further slowed? The result which one should logically have expected is a diminution in both the demand and the supply, efficiency of the circulation remaining as before. That such has not been found to be the case since the postoperative results have been analyzed does not preclude the fact that it was not predictable on the early physiologic work. Moreover the statement[13] that "with arteriosclerotic narrowing of the coronary vessels, the blood supply of the heart through these vessels may be inadequate to the needs of a normal metabolic rate although sufficient for the needs of the heart at lower metabolic rates" overlooks the fact that the slowing of the blood flow and the diminution of volume out-

put of the heart that accompanies myxedema would tend to decrease the blood supply through these same narrowed coronary arteries.

Theoretically one might have said that it would be desirable to lower the basal metabolism and at the same time maintain the rate of blood flow unchanged or to speed it up. It is clear that the only effect that could have been anticipated from the physiological studies was a further slowing of the circulation which might be harmful. May it not be that improvement will be determined by just this differential effect? When the fall in metabolism is accompanied by less than the expected slowing of blood flow, improvement should occur. As a matter of experience the velocity of blood flow has shown no constant relationship to the fall in the basal metabolism. At times when there were congestive failure and a very slow velocity of blood flow before operation, the flow remained unchanged after operation, even when the metabolism was –30 per cent, in the face of clinical improvement. When the circulation time was normal or essentially normal, as in the cases of angina pectoris and those cases of congestive heart failure which became well compensated before operation, there always was a distinct slowing of the blood flow which accompanied the fall in the basal metabolic rate. Why these different results occurred has not been thoroughly explained, although it may be that in congestive heart failure an improvement in the efficiency of the circulation following the operation brought about by some unknown mechanism of itself tends to speed up the circulation and thereby counterbalance the slowing effect that would otherwise result from the artificial myxedema.

Furthermore, the early observations on the rate of blood flow on congestive heart failure were not applicable to cases of pure angina pectoris, for here there is no congestion nor is there any slowing of blood flow. In angina it was not a matter of lowering the metabolism to meet the slow circulation. Particularly is this true of those patients who have attacks of angina at rest. Such cases seem to have some internal mechanism that explodes or acts as a trigger in precipitating attacks. Whether this is dependent on a temporary increase in the rate of blood flow has never been determined. There is much presumptive evidence that the mechanism, whatever it may be, is linked up with the adrenals.

Clinically it has been observed that certain cardiac disturbances which were in some way related to the thyroid gland were independent of the basal metabolism. Wilson and his associates[20] called attention to instances of transient auricular fibrillation occurring in patients with a normal metabolism who only subsequently developed an elevation of the basal metabolic rate and in whom the cardiac abnormality disappeared after subtotal thyroidectomy. Likewise, Coller[21] found that certain cardiac irregularities in nontoxic goiter disap-

peared after subtotal thyroidectomy although the metabolism was normal. Furthermore, it was noted in this present investigation that in patients who had daily and frequent attacks of angina, such attacks disappeared directly after the thyroidectomy, at a time when the basal metabolic rate and the rate of blood flow were still the same as they were before operation. Many patients volunteered the information that within a few days after total thyroidectomy they were less heart conscious and that mild nonanginal discomforts around the heart disappeared. From all this it was predicted that removing the thyroid gland causes a fundamental alteration in the response of the heart to adrenalin. This has since been found to be true both clinically in our cases and experimentally in animals. It has been shown that adrenalin reproduced attacks of angina if injected before operation[22] and failed to do so the second or third day after total thyroidectomy.[23] Furthermore, certain irregularities of the heart can be produced by the injection of adrenalin into rabbits that are made hyperthyroid that do not occur with similar doses in normal or thyroidectomized animals.[4] Likewise recent animal experiments have shown that there is a fundamental difference in the response of the heart to injected or secreted adrenalin after total thyroidectomy.[24] The acceleration of the heart following the same stimulus is lessened 30 to 60 per cent by such an operation. All these observations indicate that the removal of the thyroid gland alters the sensitivity of the heart to adrenalin, and confirms opinions long since expressed that the thyroid gland enhances the adrenalin effect on the body.[25, 26] These considerations are pertinent in indicating that the early theoretical data which have been supposed to be the starting point of this new operation need some revision, notwithstanding the fact that subsequent studies seem to validate this therapeutic procedure.

Very recently an investigation to explain early relief of pain in angina pectoris was published by Weinstein and his associates.[27] They presented some evidence to show that the early relief was due to the severance of nerves during the operation and that this effect was only temporary. Although it is impossible to refute these results without reproducing the experiments performed in that research (especially deliberate hemithyroidectomy), we are of the opinion that their explanation is not valid. It seems unlikely that there can be enough cardiac nerves in the operative field to account for results we have witnessed. Furthermore, the disappearance of hepatic engorgement during the first seven to ten days following operation, which we and others have observed to occur before any appreciable fall in basal metabolic rate, cannot be explained on the basis of section of cardiac nerves. At any rate much more work will be necessary to account for the effects on the circulation that follow total thyroidectomy.

Finally in considering the rationale of complete thyroidectomy one naturally must pay due regard to the possible harmful effects. When it is appreciated that the operation is proposed for conditions that are inherently progressive and that do not respond satisfactorily to the ordinary available measures, one may be ready to accept some comparatively minor handicaps that might result. The possibility of postoperative myxedema is not very material, for the administration of thyroid gland can undo, if it were desirable, most if not all the deleterious effects of this type. The danger of parathyroid tetany has been insignificant, for whatever minor symptoms of this deficiency have occurred have been readily controlled. Injury to the recurrent laryngeal nerve is a technical problem, and so far has given rise to very little concern. The operative mortality, had it been high, would have been a serious handicap. Realizing that the life expectancy in the patients subjected to this operation is not great and that sudden fatalities or other disastrous complications are the expected events in these conditions, the operative mortality of 5 to 10 per cent cannot be regarded as excessive.

The medical management of all these cases has recently been discussed[28] and need not be gone into here. There is one point, however, that needs comment. It has been urged[27] that patients with angina pectoris should be kept strictly in bed until a significant fall in the basal metabolism has occurred, because the early relief of pain was regarded as merely due to the severance of nerves. This may require several weeks of bed care in some cases, and it is no more logical than it would be to advise a patient with angina pectoris who obtained relief following cervical sympathectomy or alcohol injections of the thoracic ganglia to stay in bed for the entire time that he remains free from pain, which may be years. We have, therefore, allowed patients with uncomplicated angina to become ambulatory from a few days to a week after the operation.

SUMMARY

1. A follow-up study was made of twelve cases of severe intractable heart disease previously reported in which thyroidectomy was performed. This showed that although some benefit was obtained, the state of the lesions was so far advanced that in most cases improvement did not last an appreciable length of time.

2. A second series of thirty cases of patients also suffering from chronic intractable heart disease is now reported. There were twenty-three patients with angina pectoris and seven with congestive heart failure. Six of the latter had mitral stenosis and one was a nonvalvular case. They were all incapacitated to various degrees.

3. There were two surgical fatalities among these thirty cases, both in the anginal group. One additional patient died of typical acute coronary thrombosis five days postoperatively after he was feeling quite well and was ambulatory. A fourth died of coronary thrombosis four months after the operation, having obtained considerable improvement in the preceding three months. Of the remaining nineteen, all are still alive an average length of six months after the operation. Improvement was regarded as "excellent" in eight, "good" in six, "moderately good" in four, and "fair" in one.

Among the seven cases of congestive failure there was no surgical mortality. One patient died about five weeks after operation of mesenteric thrombosis and acute pulmonary edema. In three the result was "excellent," in two it was "good," and in one it was "fair."

4. The criteria for selection of cases were discussed. At present, there still remains some uncertainty as to the exact type of case with congestive heart failure that is suitable for this procedure.

5. Observations were made, particularly in the cases with angina pectoris, of the following factors: the basal metabolic rate, the velocity of blood flow, the cholesterol content of the blood, the size of the heart, the blood pressure levels, the possibility of secondary anemia, the body weight, the vital capacity of the lungs, and the electrocardiograms.

6. The rationale of this procedure and some theoretical considerations that underlie it are discussed. It was thought that apart from the main effect of thyroidectomy in diminishing the work of the heart by decreasing the basal metabolic rate there was an additional important effect, i.e., the diminution in the sensitivity of the heart to adrenalin.

7. The results obtained in this study indicate that total thyroidectomy produced specific clinical improvement in cases that were refractory to the ordinary methods of treatment. This seemed to be much more definite in those with angina pectoris than in those with congestive heart failure. This operation should be undertaken, however, only after the most careful consideration of the diagnosis and prognosis. Furthermore, it must be evident that ordinary medical management has failed and that the operation is likely to result in improvement that is otherwise unobtainable.

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CORONARY ARTERIOSCLEROSIS, CORONARY THROMBOSIS, AND THE RESULTING MYOCARDIAL CHANGES

An Evaluation of Their Respective Clinical Pictures Including the Electrocardiographic Records, Based on the Anatomical Findings*†

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(Continued from page 595 of June issue)

DISCUSSION OF THE ANATOMICAL FINDINGS

References to the literature of anatomical lesions are only occasionally given in this discussion. The articles by Kirch,[7] by Benson[8] and by Karsner,[6] should be consulted for a review of the more modern literature of this subject.

In the present series, as mentioned previously, all major branches of the coronary arteries were carefully dissected with small scissors and the lesions in each heart recorded in a separate diagram. Fig. 1 shows a diagram of the course of the coronary arteries adapted from illustrations given by Spalteholz[9] and by Gross[10]‡ with the nomenclature of the coronary branches as used by Spalteholz.§ This diagram served as a model for the individual diagrams accompanying the case reports.

Types of Lesions in the Coronary Arteries.—The most commonly encountered lesions were marked fibrosis, hyalinization, calcification, and thrombi. The various stages of coronary sclerosis described by Bork[11] were encountered with the exception of the first, the earliest stage. There was marked intimal hyperplasia with lipoid deposits, atheromatous formations, and calcification of the intima and to a lesser extent of the media. No attempt was made to differentiate between occlusions resulting from hyalinized and calcified plaques and so-called connective tissue occlusions as described by Koch and Kong[12] because of the impossibility of differentiating the latter type of occlusions from those caused by organized thrombi. Table I gives a summary of the types

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‡We are indebted to Dr. N. Mitchell for making this diagram for us.

§Instead of right coronary artery, the term "right circumflex branch" is used to signify the homologous character of this vessel to the circumflex branch of the left coronary artery.

of lesions in the various branches of the coronary arteries. Recent thrombi of the coronary arteries were found 18 times, while organizing and old thrombi were encountered in 14 instances. Occlusions by calcified plaques were encountered 13 times. Every heart showed more than one occlusion or marked narrowing of the coronary arteries. In some instances as many as four lesions were found in the coronary arterial system in a single heart. This emphasizes the importance of dissecting all main branches of the coronary arteries even after one occluding lesion has been demonstrated.

There was no relation between the gross lesions in the larger branches and the histological changes in the smaller branches (arterioles). Often the latter vessels showed no noteworthy changes in the presence of marked arteriosclerosis of the larger branches. In only a few instances did the sections of the myocardium reveal intimal thickening of the arterioles. None of the sections, however, showed changes characteristic of obliterating endarteritis. Occasionally a moderate infiltration of round cells and endothelial cells was found in the perivascular spaces, but in no instance was there evidence of syphilis of the coronary arteries.

In the 32 instances in which thrombi were encountered in the coronary arteries, the thrombi were located on atheromatous ulcers. The sections revealed either recent thrombi which showed no evidence of organization or organizing thrombi with partial replacement by connective tissue. In some sections much calcification was found, while others revealed typical atheromas in the subintimal layers of the coronary arteries.

Location of Coronary Lesions.—In all instances both coronary arteries were involved, but most frequently the more severe lesions were found in the left coronary artery, especially in its descending branch about 2 to 3 cm. from its origin. The next most severely affected branch of the left coronary artery was the ramus anterior ventriculi sinistri. The occluding point was often demonstrated in an area about 1 cm. distal to its mouth. The ramus marginis obtusi was involved eight times. The circumflex branch of the right coronary artery was narrowed in 22 instances and occluded by calcified plaques in only one instance; the more severe lesions were found in an area about 3 cm. distal to its mouth. Thrombi in the coronary arteries were found most frequently where the arteriosclerotic lesions were most marked, namely, in the descending branch of the left coronary artery. Thrombi were found in this artery in 14 instances. The posterior descending branch revealed thrombi in two, and marked arteriosclerotic changes in five instances. It may be mentioned in this connection that in five cases this branch came off the left coronary artery, and in only two of these five instances was it free from changes.

TABLE I

CASE	RIGHT CORONARY ARTERY		LEFT CORONARY ARTERY				HEART	TYPE OF DEATH
	RIGHT CIRCUMFLEX BRANCH	POSTERIOR DESCENDING BRANCH	ANTERIOR DESCENDING BRANCH	LEFT CIRCUMFLEX BRANCH	RAMUS VENTRICULI SINISTRI ANTERIOR	RAMUS MARGINIS OBTUSI		
I	Marked narrowing by calcified plaque	Recent thrombus	Occlusion by calcified plaque					Sudden
II	Almost complete obliteration by calcified plaque		Occlusion by calcified plaque		Almost complete obliteration by calcified plaque		Aneurysm involving apical portion of left ventricle	Sudden
III	Recent thrombus					Occlusion by calcified plaque	Recent infarct in latero-posterior wall of left ventricle	Sudden
IV	Almost complete obliteration by calcified plaque		Recent thrombus		Occlusion by calcified plaques		Recent infarction involving apical portion of l. ventricle	Sudden
V	Organizing thrombus		Recent thrombus (Main stem)					Sudden
VI	Organized thrombus. Marked narrowing by calcified plaque		Recent thrombus	Marked narrowing by calcified plaques				Sudden
VII	Recent thrombus		Marked constriction by calcified plaque		Old occlusion by arteriosclerotic plaques	Old occlusion by arteriosclerotic plaque	Recent infarct in latero-posterior portion close to base	Sudden
VIII	Almost complete obliteration by calcified plaque		Occlusion by calcified plaques		Occlusion by calcified plaques		Recent infarct involving apical portion of l. ventricle	Gradual

TABLE I—CONT'D

IX	Almost complete obliteration by calcified plaque		Recent thrombus		Old occlusion by calcified plaque		Recent infarct involving apical portion of left ventricle	Gradual
X	Narrowing by calcified plaques		Recent thrombus	Narrowing by calcified plaques	Narrowing by calcified plaques		Infarct involving anterior wall of left ventricle	Gradual
XI	Marked sclerosis with narrowing by calcified plaques		Recent thrombus	Almost complete obliteration by calcified plaque			Infarct involving lower half of septum, apex and anterior wall	Gradual
XII	Almost complete obliteration by calcified plaques		Almost complete obliteration by calcified plaque		Almost complete obliteration by calcified plaque		Old infarct with aneurysmal dilation in apex	Sudden
XIII	Almost complete obliteration by calcified plaques		Recent thrombus		Almost complete obliteration by calcified plaque		Recent infarct involving anterior wall of l. ventricle and septum	Gradual
XIV	Almost complete obliteration by calcified plaque	Branch of l. cor. art.	Almost complete obliteration by calcified plaque		Recent thrombus		Recent infarct in lateral wall of left ventricle	Sudden
XV	Recent thrombus			Complete obliteration by calcified plaques			Recent infarct in left ventricle close to base	Gradual
XVI	Marked narrowing by calcified plaque		Organizing thrombus		Marked narrowing by calcified plaque		Old and recent infarcts, apic., port., l. vent., and septum	Gradual
XVII	Narrowing by calcified plaque		Organizing thrombus	Narrowing by calcified plaque				Gradual
XVIII	Recent thrombus	Marked constriction by arteriosclerotic plaques	Marked constriction by arteriosclerotic plaques	Marked constriction by arteriosclerotic plaque			Old infarct, apex and recent infarct, base of l. ventricle	Sudden

TABLE I—CONT'D

CASE	RIGHT CORONARY ARTERY		LEFT CORONARY ARTERY				HEART	TYPE OF DEATH
	RIGHT CIRCUMFLEX BRANCH	POSTERIOR DESCENDING BRANCH	ANTERIOR DESCENDING BRANCH	LEFT CIRCUMFLEX BRANCH	RAMUS VENTRICULI SINISTRI ANTERIOR	RAMUS MARGINIS OBTUSI		
XIX	Marked constriction by calcified plaque			Organized thrombus			Old infarct in left ventricle close to base	Gradual
XX	Almost complete obliteration by calcified plaque			Marked narrowing by calcified plaque		Organized thrombus	Organizing infarct in latero-post. wall of l. ventricle	Sudden
XXI	Marked narrowing by arteriosclerotic plaque	Marked narrowing by arteriosclerotic plaques	Recent thrombus at point of division into these two branches				Recent infarct in apex, rupture and hemopericardium	Sudden
XXII		Branch of l. cor. art. Marked narrowing by calc. pl.	Almost complete obliteration by calcified plaques	Marked narrowing by calcified plaques			Organizing infarct in latero-post. wall of left ventricle	Gradual
XXIII	Complete obliteration by calcified plaque		Marked narrowing by calcified plaque				Old infarct in apex of left ventricle	Gradual
XXIV	Narrowing by calcified plaque		Organizing thrombus		Obliteration by arteriosclerotic plaques		Organizing infarct in apex of left ventricle	Gradual
XXV		Branch of l. cor. art. Marked narrowing by calc. pl.	Organizing thrombus		Marked narrowing by calcified plaques	Marked narrowing by calcified plaques	Organizing infarct in anterior wall of left ventricle	Sudden

TABLE I—CONT'D

XXVI	Marked narrowing by calcified plaques		Organizing thrombus	Marked narrowing by calcified plaques			Organizing infarct in apex of left ventricle	Gradual
XXVII		Old thrombus	Narrowing by calcified plaques	Narrowing by calcified plaque		Narrowing by calcified plaque	Old infarct (aneurysm) in post. wall of left ventricle	Gradual
XXVIII	Constriction by calcified plaques		Recent thrombus and organized thrombus	Constriction by calcified plaques	Constriction by calcified plaque	Constriction by calcified plaques	Two aneurysms, one in apex, one in base of left ventricle	Sudden
XXIX	Narrowing by calcified plaques	Branch of l. cor. art.	Old thrombus	Recent thrombus	Almost complete obliteration by calcified plaque	Almost complete obliteration by calcified plaque	Organ. infarct in ant. wall at apex, old infarct in lat.-post. base of l. ventricle	Sudden
XXX	Arteriosclerotic plaques		Organizing thrombus	Almost complete obliteration by calcified plaque		Almost complete obliteration by calcified plaque	Organizing infarct with aneurysm in apex of l. ventricle	Sudden
XXXI	Recent thrombus		Complete obliteration by calcified plaque	Narrowing by calcified plaque	Narrowing by calcified plaque		Old infarct with aneurysm in anterior wall of l. ventricle	Sudden
XXXII	Narrowing by calcified plaques	Narrowing by calcified plaques	Marked narrowing by calcified plaques	Marked narrowing by calcified plaques	Marked narrowing by calcified plaques		Old infarct in the anterior walls of r. and l. ventricles	Gradual
XXXIII	Recent thrombus		Marked narrowing by calcified plaques	Marked narrowing by calcified plaques	Old thrombus		Old infarct in the apex of the left ventricle	Sudden
XXXIV	Marked narrowing by arteriosclerotic plaque	Branch of l. cor. art. Almost comp. obl. by calc. pl.	Almost complete obliteration by calcified plaque		Almost complete obliteration by art. scl. plaque		Recent infarct in anterior wall of left ventricle	Gradual

In some instances the thrombus did not cause a sudden occlusion of the lumen, but was at first mural in type. Later, the thrombus apparently increased in size and eventually occluded the lumen. This could be demonstrated in the histological sections by observing an older thrombus close to the wall of the artery at one side, with the more recent thrombus adjacent to it.

Levine and Brown[2] stated that in 39 of their 45 autopsy cases, the infarction of the myocardium was found within the distribution of the descending branch of the left coronary artery. They also noted that when the anterior descending or the circumflex branches of the left coronary artery were the involved vessels, the occlusion was usually found about 2 cm. distal to the bifurcation of these branches. This region was also recognized by Mönckeberg[13] as the seat of the severest changes of the coronary arteries. Kirch[7] referred to this location as "Lieblingsstelle" (place of predilection). It may be said in this connection, however, that other investigators, like Bork[11] and, very recently, Barnes and Ball,[14] do not agree that the left coronary artery is more frequently involved than the right. The latter investigators believe that the designation of the anterior descending branch of the left coronary artery as "the artery of coronary occlusion" is not justifiable. Wolkoff[15] in an extensive study on coronary arteriosclerosis, however, has shown that the left coronary artery is more commonly involved than the right and that the changes are more pronounced in its distal portions. She maintained that the point of division in the smaller branches and, more commonly, those portions of the walls of the vessels which are directly attached to the myocardium are the sites of predilection. This author believes that the arteriosclerotic lesions at branching points are the result of the pressure directed against these areas.

Analysis of our material fails to reveal why the descending branch of the left coronary artery presents the more frequent and severe lesions. We could not demonstrate any single point as the one most commonly involved, but found the involvement confined mostly to an area approximately 1 cm. in length beginning about 2 cm. from the point of origin of the descending branch. This would speak against pressure exerted upon branching points as the cause of arteriosclerosis, because the lesions were not confined to the branching points but occurred in wider areas.

Myocardial Lesions.—Depending upon the relative age of the myocardial lesions, various changes were found. In every instance, however, much fibrosis was present in the myocardium, and was especially noticeable in the perivascular spaces. The connective tissue was usually poor in nuclei, and many of the fibers were hyalinized.

One of the most striking findings in this series of hearts was the fact that whenever a myocardial infarct was encountered, at least two branches of the coronary arteries supplying the infarcted area were involved. In this consecutive series of cases no instance was found in which myocardial infarction occurred with only one main artery involved. The involved branches were either completely occluded by calcified plaques or thrombi, or extremely narrowed by calcified plaques. Where extreme narrowing only was present, at least three main branches were involved.

The infarcted areas in general were present in those regions which were supplied by the diseased branch of the coronary artery. The most common site, therefore, was the apical region of the heart. Sometimes parts of the septum were involved. Less frequently, the posterior wall of the left ventricle showed infarcts. In a few instances infarcts were found in both of these regions. In only one instance was an infarct noted in the anterior wall of the right ventricle. Occasionally a recent thrombus was found in one coronary artery, while the recent infarct was found in an area supplied by the opposite coronary artery. In three instances (Cases III, VII, and XX) the infarcts were found in the lateroposterior wall of the left ventricle close to the base. In Case XX, the supplying branch, the ramus marginis obtusi of the left coronary artery, was occluded by a recent thrombus, and the circumflex branch of the right coronary artery showed an almost complete occlusion by calcified plaques. In Cases III and VII, however, the ramus marginis obtuse was occluded by an old calcified plaque. In each, the infarct, being very recent, could not have been the result of this old occlusion. The circumflex branch of the right coronary artery revealed a recent thrombus. The area, normally supplied by the ramus marginis obtusi, must have been supplied in these instances prior to the recent occlusion by collaterals originating from the right coronary artery. In these two cases, therefore, the thrombus of the circumflex branch of the right coronary artery had caused an infarct in an area which originally was supplied by a branch of the left coronary artery.

In Cases XII, XXII, XXXII, and XXXIV myocardial infarcts were present, but none of the branches of the coronary arteries was occluded, although their lumina were markedly narrowed. The occurrence of these infarcts may be explained by the assumption that prior to the development of the infarcts the heart muscle was temporarily insufficient resulting in a lowering of the arterial blood pressure so that the area could not be adequately supplied with blood. We believe that the infarcts developed as a result of this temporary lack of blood supply.

Sections which were taken from the recent infarctions revealed only bare outlines of muscle fibers which showed a loss of their nuclear staining quality. In many instances, however, the connective tissue nuclei were still recognized, and the walls of the smaller blood vessels had escaped necrosis. In large recent infarcts, however, neither connective tissue nor vessel wall was preserved. Very occasionally, these changes were the only ones which could be found, a reactive process being absent. The first evidence of a reaction of the surrounding tissue to necrosis was a marked hyperemia with capillary enlargement and a moderate extravasation of red blood cells. The hyperemia in some instances was so marked as possibly to justify the term "red infarcts." In smaller infarcts, the hemorrhagic type was more noticeable than in the large ones. The recent infarcts also showed a polymorphonuclear leucocytic reaction; first, surrounding the dead muscle fibers and, later, invading the infarcted areas. In some fields these infiltrations gave the impression of an acute pyogenic inflammation. Wearn[16] has also called attention to such infiltrations. We cannot emphasize too strongly the occurrence of polymorphonuclear leucocytic infiltrations in infarcted regions because their presence in the myocardium in cases of sudden death is sometimes erroneously taken as evidence of so-called "malignant syphilitic myocarditis."

In many sections pigment granules were found either free in the tissue or in the cytoplasm of endothelial cells. The granules gave a positive iron reaction and were taken as evidence of old hemorrhage.

The histological picture of old infarcts is well known. One interesting finding, however, may be especially mentioned. In addition to old areas of fibrosis, large areas were often seen in which outlines of heart muscle fibers were still recognizable even though the fibers seemed to have been replaced by a material resembling old hyaline. Occasionally recent, organizing and healed infarcts were seen in a single section. This was observed more frequently when the infarcts were the result of occlusion of the vessel by arteriosclerotic plaques. These findings seem to indicate that the myocardial lesions, like the lesions in the coronary arteries, were progressive in nature.

It is known that the heart muscle fibers show very little tendency toward regeneration. Kaufmann,[17] however, described attempts at regeneration (Regenerationsanläufe) in the vicinity of myocardial infarcts. Such attempts, he believed, were indicated by the findings of so-called muscle giant cells close to the infarcted portions. It is, of course, questionable whether such giant cells really represent attempts at regeneration, or whether they should be classified as foreign body giant cells, the result of myocardial necrosis. In none of our sections were we able to observe giant cells. The only evidence of a compen-

satory reaction of the myocardium in the vicinity of the infarcted areas was an apparent hypertrophy of muscle fibers.

There were six instances of cardiac aneurysms. The larger aneurysms were bulging, and consisted of thin layers of fibrous tissue ("chronic aneurysms"). The endocardium in the region of the aneurysms was thickened and was often covered by thrombi. In one instance a recent infarct led to rupture and hemopericardium resulted. Occasionally, however, before the heart was opened, circumscribed thin depressed areas were noted, which projected into the ventricular cavity. These areas, obviously aneurysms in respect to their pathogenesis and histological appearance, were inverted at autopsy because of the loss of the positive intraventricular pressure. The endocardium corresponding to these inverted areas was thickened but free from thrombi.

In a number of instances infarcts were found in the left ventricle, which were silent clinically; that is to say, there was no history of attacks of pain or other symptoms suggestive of infarction, nor did cardiac insufficiency develop. This point was stressed very recently by Koch and Kong,[12] who stated that cardiac damage and cardiac insufficiency do not go hand in hand. These authors stated various reasons for the relative harmlessness of infarcts located in the anterior wall of the left ventricle. It might be possible that these regions are "silent" areas. In our series, however, there were three instances of infarcts involving the posterior wall of the left ventricle which also did not reveal clinical symptoms.

Collaterals of the Coronary Arteries.—In our series, several instances were encountered of occlusion of a main branch of the coronary artery either by an arteriosclerotic plaque or by an organized thrombus, but without infarction of the myocardium. This clearly indicates that the regions supplied by the occluded vessel must have received their blood supply from other sources. Gross[10] has shown that there is an increase of collateral anastomoses with advancing age. The age group of our series (forty-five to seventy-six years) justifies the assumption that collateral anastomoses were present which must have supplied the areas deprived of their normal arterial supply.

As to the question whether Thebesian vessels might have prevented the infarctions in some of our hearts, the following might be said: Direct communications between the coronary vessels and the ventricular cavities do exist. It has been recently shown (Bohning, Jochim and Katz[18]) that bismuth and bacteria may enter the coronary system via the Thebesian vessels in the beating heart. It still, however, remains to be proved whether or not these Thebesian vessels can supply the myocardium to any large extent when the coronary arteries are occluded. Though it is well known that a gradual occlu-

sion of one or both openings of the coronary arteries, as seen so often in instances of syphilitic aortitis, may occur without myocardial infarction, it still is possible that there is another entrance to the coronary circulation which has not received enough attention. Langer[19] in 1880 and v. Redwitz[20] in 1909 had pointed out such extracardiac anastomoses. Smetana[21] recently has shown anastomoses between the vasa vasorum of the aorta and the coronary arteries. A widespread extracardiac coronary collateral circulation was described recently by Hudson, Moritz and Wearn.[22] These authors also stated that this collateral circulation is probably of significance in compensating for sclerosis of the large trunks of the coronary arteries. Such arterial communications in cases of gradual occlusion of the coronary arteries may prevent infarctions. Special attention to such anastomoses is being given to autopsy material, the results of which will be published in the future. In our series, the absence of infarctions can be explained solely by existing anastomoses between the coronary arteries. The fact that at least two main branches of the coronary arteries were involved when infarcts were present supports this view.

Type of Death.—An attempt was made to correlate the type of death with the anatomical lesions. The cause of death in three patients who died suddenly was undoubtedly thrombosis of a main branch of one coronary artery, the main branch of the opposite coronary artery having been already occluded by an old arteriosclerotic plaque. Once the recent thrombus was found in the right coronary artery (Case I), while in two instances the recent thrombus was found in the left (Cases V and VI). These patients showed no myocardial infarctions, death having occurred before the infarcts could be established. Such a death must be considered as being the direct result of coronary thrombosis. We have not encountered a single case in this series in which death occurred suddenly as the result of the occlusion of a single main branch. It seems as though in this age group (forty-five to seventy-six years) the closure of a single main branch of the coronary system does not cause instantaneous death provided the other branches are patent. Moreover, as Case XVII reveals, a thrombus in the main branch of one coronary artery does not necessarily lead to an infarct in the heart, presumably because of a well-developed collateral circulation.

In the remaining instances death ensued as a result of myocardial incompetence in the great majority associated with myocardial infarction. Though the infarcts were caused by the lesions of the coronary artery (either thrombosis or arteriosclerotic occlusion), such lesions were not the direct cause of death. These patients survived the coronary occlusion for various lengths of time but died later of the myocardial damage. Since such an impaired myocardium may become

insufficient either gradually or suddenly, the patients with myocardial infarcts may die suddenly or succumb slowly. Sixteen patients of this group succumbed gradually, and fifteen died suddenly. In some instances the final factors which led to a sudden greater demand upon the heart just before death could be deduced. The use of a bedpan, a sudden attempt to leave the bed, or other physical strains (perhaps psychic upsets) must have called for a sudden increase of work of the heart to which the impaired myocardium could not respond and the patient died instantaneously.

Angina Pectoris in the Light of the Anatomical Findings.—Eighteen patients revealed attacks which clinically were typical of angina pectoris. A number of these patients revealed thrombosis of the coronary arteries, arteriosclerotic occlusion of the coronary arteries, and also myocardial infarctions. Yet similar conditions were found in the hearts of patients who neither revealed clinical evidence of angina pectoris nor gave a history of such a syndrome. Moreover, severe arteriosclerosis of the coronary arteries and even myocardial infarctions were found at autopsy in patients who had had no symptoms of heart disease. Therefore, it seems untenable to explain angina pectoris on the basis of coronary thrombosis, coronary sclerosis, or myocardial infarction per se.

A large number of clinicians still explain angina pectoris on the basis of spasm of the coronary arteries and the resulting myocardial ischemia. From the point of view of the morphologist, nothing can be said for or against spasm of the coronary arteries as the cause of angina pectoris because evidence cannot be obtained of the existence of spasm in the gross or histological picture. It seems difficult, however, to understand how a vessel wall, markedly thickened as a result of arteriosclerosis and often presenting calcified walls, could be subjected to temporary spasm. From a morphological point of view we also have no means of evaluating or confirming ischemia as a cause of angina pectoris, although we are aware of the experimental work indicating it as a possible cause.

Büchner[23] recently reported ten patients with angina pectoris who died shortly after their attacks. Autopsies revealed infarcts of the myocardium in every instance, although some of these could be detected only by a microscopical examination. He concluded that these latter infarcts were of importance in considering the anatomical equivalent of angina pectoris. In our material a detailed histological examination of the myocardium from blocks cut from various portions of the hearts failed to disclose evidence of such infarcts in hearts of patients who had had typical attacks of angina pectoris. We feel that sufficient portions of the myocardium were examined in a sufficient number of cases with negative results to rule out the possibility of

minute infarcts having caused every attack of angina pectoris. We do not believe that a myocardial infarct, although minute, is the necessary anatomical equivalent of angina pectoris.

One possible explanation for the attacks of angina pectoris may be constructed from this study. All our cases revealed coronary lesions and resulting myocardial damage. While we cannot believe, as mentioned before, that a rigid coronary artery may be subjected to spastic contractions and resulting ischemia, it might be possible that the damaged heart in these instances develops a temporary insufficiency. In every instance of angina pectoris a damaged myocardium could be demonstrated severe enough to explain a temporary insufficiency. The damage is not necessarily caused by an infarct, but may be caused by simple myocardial fibrosis. The final causes for a temporary myocardial insufficiency may be insignificant. As a result of the insufficiency, the arterial blood pressure is lowered, the heart output is decreased, and the blood supply through the narrowed coronary arteries is interfered with. The momentary decrease of coronary blood supply or its effects, whether ischemia, dilatation of the postcapillary veins or the compensatory adjustment of the heart, etc., may be responsible for angina pectoris.

DISCUSSION OF ELECTROCARDIOGRAMS

Following the work of Herrick,[24] Smith[25, 26, 27] and Pardee,[28, 29] it has been generally accepted that characteristic changes in the electrocardiogram result from recent coronary occlusions. The earliest change is a noticeable deviation of the S-T segment from the isoelectric level. Later the S-T segment becomes isoelectric, shows a residual convexity, and is followed by a pointed T-wave with rounded shoulders and symmetrical limbs. The direction of the T-wave is opposite to the original deviation of the S-T segments. In succeeding records the size of this T-wave waxes and wanes, and eventually the T-wave may disappear. Parkinson and Bedford[30] pointed out that the serial changes in the electrocardiogram, with rare exceptions, can be placed in one of two groups. Early in the first group, the so-called T_1 type, the S-T segment is elevated in Lead I and depressed in Lead III; later the T-wave in Lead I becomes negative. Early in the second group, the so-called T_3 type, the S-T segment is elevated in Lead III and depressed in Lead I; later the T-wave in Lead III becomes inverted. Bohning and Katz[31] have called attention to the development of a large, upright T-wave in Lead III in type T_1 and in Lead I in Type T_3. Recently, Wilson and his coworkers[32] attempted to classify electrocardiograms following coronary occlusion into two groups, depending upon the lead in which a large negative Q-wave appeared. In the Q_1 type this negative Q-wave is found in Lead I, and there may be a large nega-

tive S-wave in Lead III; in the Q_3 type this negative Q-wave is found in Lead III, and a negative S-wave may appear in Lead I. The literature contains instances of recent coronary occlusion where the electrocardiographic findings do not fit into the characteristic Q or T patterns. Furthermore it is not always easy to classify the Q-T type.

Barnes and Whitten[33] concluded that the changes in the electrocardiogram depended upon the location of the infarct. They found that the T_1 type is characteristic of infarction of the anterior wall and apex of the left ventricle, and the T_3 type of infarction of the posterior wall of the left ventricle. This conclusion has been confirmed by several authors (cf. Rose and Meyers,[34] Wood and his associates.[35] However, Gilchrist and Ritchie,[36] after comparing the electrocardiograms with autopsy findings in published cases, concluded that the available evidence does not support the view that the form of the electrocardiographic record is a reliable guide in locating the site of the infarct. Wilson and his coworkers,[32] after surveying their material, state "that the location of the infarct plays a most important rôle in determining the form of the ventricular complex in coronary occlusion is scarcely to be doubted. When an attempt is made, however, to correlate the one with the other . . . . many puzzling cases are met with." They found a number of instances both in their own series and in those reported in the literature where the infarct was not located in the region anticipated from the type of the electrocardiogram. Fenichel and Kugel[37] have suggested that a large inverted Q_3-wave is due to infarction of the posterior portion of the ventricular septum.

Gilchrist and Ritchie[36] pointed out that while rapid changes in the ventricular complex in serial electrocardiograms are strong presumptive evidence of myocardial infarction, similar changes developing over a long period of time may be due to progressive myocardial fibrosis following coronary sclerosis. It is now well recognized that ectopic rhythms, such as premature systoles, paroxysmal tachycardia, paroxysmal auricular fibrillation or flutter and terminal ventricular fibrillation, follow recent coronary occlusions. Partial or complete A-V block and intraventricular block (bundle branch or arborization types) also may follow recent coronary occlusion. Smith[27] and Wearn[16] have found small amplitude of the QRS complexes after a recent coronary occlusion.

Many of the views concerning changes in the electrocardiogram following recent coronary occlusion are based to a large extent on a correlation of the records with the clinical findings alone; no autopsies having been performed to confirm the clinical interpretation. This study, however, has shown, as mentioned above, that lesions expected from the clinical picture are not always found at autopsy. Further-

TABLE II

SUMMARY OF ELECTROCARDIOGRAPHIC FINDINGS

CASE	TIME EKG TAKEN			DOES IT INDICATE RECENT CORONARY OCCLUSION?	AXIS DEVIATION	BLOCK PRESENT	Q TYPE	T TYPE	DOES IT CORRESPOND WITH		LOW AMPLITUDE PRESENT	ECTOPIC RHYTHMS	LOCATION OF INFARCT WHEN RECORD TAKEN
	BEFORE INFARCTION	SOON AFTER INFARCTION	SOME TIME AFTER INFARCTION						WILSON'S CLASSIFICATION OF Q TYPE	BARNES AND WHITTEN'S CLASSIFICATION OF T TYPE			
VII	Yes			No	Left	None	3	3			No	Auricular extra.	None present
VIII 1st	Yes			No	Left	Intraventricular common type bundle	?	?			No	Ventricular extrasystoles	None present
XIII 1st	Yes			Compatible with late stage	Left	None	?	3			No	None	None present
XIV	Yes			Yes	Left	None	3	3			Yes	None	None present
XVII	Yes			No	Left	None	1(?)	?			No	None	None present
XVIII 1st	Yes			No	Left	None	?	?			No	None	None present
XX 1st	Yes			No	None	None	?	3(?)			No	None	None present
XXIV	Yes			Suggestive in view of history	Left	None	1	1			Yes	Sinus tachycardia	None present
XXXIV 1 and 2	Yes			No	Left	None	3	3			No	Auricular fibrillation	None present

TABLE II—CONT'D

XXXIV 3	Yes			Suggestive in view of history	Left	None	3	3			No	Auricular fibrillation	None present
II 2nd			Yes	Suggestive in view of first record	Left	Intraventricular common type bundle	?	3	?	No	No	Nodal rhythm	Anterior apex
XII			Yes	No	None	None	1	?	Yes	?	No	Auricular extrasystoles	Anterior apex and anterior septum
XVIII 3 and 5			Yes	No	Left	None	?	?	?	?	No	Ventricular extrasystoles	Anterior apex
XXVIII			Yes	No—but compatible	None	None	1	?	Yes and No	?	Yes	Ventricular extrasystoles	1. Anterior apex 2. Posterior base
XXX			Yes	No	None	Intraventricular indeterminate	?	?	?	?	No	None	Anterior apex and anterior septum
III		Yes		Suggestive in view of history	Left	Intraventricular common type bundle	3	3	Yes	Yes	No	Auricular fibrillation; ventricular extrasystoles	Posterior base
IV		Yes		No—but compatible in view of history	Right	None	?	?	?	?	Yes	None	Anterior apex and anterior septum

TABLE II—CONT'D

CASE	TIME EKG TAKEN			DOES IT INDICATE RECENT CORONARY OCCLUSION?	AXIS DEVIATION	BLOCK PRESENT	Q TYPE	T TYPE	DOES IT CORRESPOND WITH		LOW AMPLITUDE PRESENT	ECTOPIC RHYTHMS	LOCATION OF INFARCT WHEN RECORD TAKEN
	BEFORE INFARCTION	SOON AFTER INFARCTION	SOME TIME AFTER INFARCTION						WILSON'S CLASSIFICATION OF Q TYPE	BARNES AND WHITTEN'S CLASSIFICATION OF T TYPE			
VIII 2nd		Yes (May have been just before)		Suggestive in view of first record	Left	Intraventricular common type bundle 1st degree A-V	3	3	No	No	No	Ventricular extrasystoles	Anterior apex and anterior septum
IX		Yes		No	Left	Intraventricular common type bundle	?	1(?)	?	?	No	Auricular flutter in second record	Anterior apex and anterior septum
XI		Yes		No	Left	None	?	1(?)	?	?	No	Ventricular extrasystoles	Anterior apex and anterior septum
XIII 2 and 7		Yes		Yes—in view of first record	Left	None	1	1(?)	Yes	Yes (?)	No	None	Anterior apex and anterior septum
XVIII 2		Yes		Yes—in view of previous record	Left	None	1	3	Yes	No	No	None	Anterior apex

TABLE II—CONT'D

XVIII 6		Yes	Yes	Yes—in view of previous record	Left	None	?	3	?	Yes	Yes	Ventricular extrasystoles, sinus tachycardia	1. Posterior base (recent) 2. Anterior apex (old)
XX 2 and 3		Yes		Yes—in view of previous record	None	None				Yes	Yes	Sinus tachycardia	Posterior base
XXV		Yes		Yes	None	None	1	3(?)	Yes	No (?)	Yes	None	Anterior apex
XXVI		Yes		Yes—because of change in three records	1st right	Intraventricular uncommon type bundle	3	3	No	No	No	Sinus tachycardia	Anterior apex and anterior septum
XXIX		Yes	Yes	Yes—in view of history	None	Intraventricular arborization type	3	3	No (recent) Yes (old)	No	Yes	Ventricular extrasystoles	1. Anterior apex (recent) 2. Posterior base (old)
II 1st	?	?	?	No	Left	Intraventricular common type bundle	?	3			No	None	Possibly anterior apex
XXIII	?	?	?	No	Left	1st degree A-V block	?	?			No	None	Possibly anterior apex

more, neither coronary thrombosis nor myocardial infarction always gives characteristic clinical evidence. The electrocardiographic findings in the present study, therefore, were correlated with the changes found at necropsy. The apparent duration of the thrombosis or infarction was determined by gross and histological examination. With this information we could determine, with reasonable certainty, whether the electrocardiogram was taken before, shortly after, or some time after, the myocardial infarction (or coronary thrombosis) had occurred. The findings are assembled in Table II. Since the study started at the autopsy table, it was not surprising to find that for a variety of reasons electrocardiograms had not been taken in a number of instances and had not been taken often enough in others.

Of the 34 patients studied, 21 had one or more electrocardiograms. Of these, ten were taken before infarction occurred; five were taken a long time after infarction occurred; twelve were taken soon after infarction. At the time two of the last twelve records were taken an old infarct was present in addition to the recent one. The time relationship between the electrocardiogram and the infarct could not be determined in two other instances.

Electrocardiograms Taken Before Infarction.—The electrocardiograms taken before infarction occurred might be expected to show only the changes caused by advanced coronary sclerosis and myocardial fibrosis. Four of these records, however, either suggested a recent coronary occlusion or at least were compatible with such a lesion (record 1 of Case XIII, Cases XIV and XXIV, and record 3 of Case XXIV). Case XIV is particularly noteworthy in this regard. The record showed a typical early Q_3-T_3 type with low amplitude, but no infarct was present. The record in Case XXIV, and the third record in Case XXXIV not only had suggestive changes in the electrocardiogram but suggestive histories as well, and yet no infarcts were present at the time the records were taken.

Electrocardiograms Taken Some Time After Infarction.—Of the five cases in which the records were taken some time after infarction had occurred, three showed nothing characteristic of such an event. The intraventricular block in the second record of Case II and in the record of Case XXX is not necessarily an indication of infarction, since it also occurs in this series when infarcts were not present (record 1 of Case VIII). Low amplitude which was found once in the presence of infarction is not characteristic, since it was found in Cases XIV and XXIV when no infarcts were present. Premature systoles were also found in Cases VII and VIII before infarction had occurred.

It was not easy to determine the Q-T type in the records taken a long time after infarction had occurred. Two of the five showed a Q_1 type, one associated with an infarct in the anterior wall, the other

with an infarct in both the anterior and the posterior wall of the left ventricle. In the other three instances the Q-type could not be determined; the infarct in each of these involved the anterior wall. The T-type could be determined only once. In this instance the type was T_3, although the infarct was located in the anterior wall of the left ventricle.

Electrocardiograms Taken Soon After Infarction.—According to the age of the infarct as determined from the morphological picture, records (or series of records) were taken in 12 instances soon after the development of the infarct. In two of these (Cases IX and XI) the records were not at all characteristic of recent coronary occlusion. In the other ten cases the records either were characteristic of recent coronary occlusion, or at least suggested such a lesion when correlated with the clinical findings or when compared with the records taken previously.

Intraventricular block of various types was present in Cases III, VIII, IX, XXVI and XXIX; in Case VIII a first degree A-V block was also noted. The nature of the intraventricular block bore no relation to the location of the infarct. Involvement of the anterior portion of interventricular septum occurred without block (Cases XI and XIII), with the uncommon type of bundle-branch block (Case XXVI), and with the common type of bundle-branch block (Cases VIII and IX). Involvement of the posterior wall of the left ventricle was associated with the common type of bundle-branch block in Case III; but in Case XX a similarly located infarct was not associated with intraventricular block. It must be remembered, however, that in many instances the intraventricular block may have been present before the infarct occurred, and might have been due to advanced coronary sclerosis and myocardial fibrosis.

Ectopic rhythms were no more frequent in this group of cases than in the preceding two groups. Low amplitude occurred more frequently in this group (5 out of 12 times) than in the other two groups. Left axis deviation was present in seven of these twelve cases, in three no deviation was found and in two the deviation was to the right. Left axis deviation, however, was also frequently seen in records obviously taken before infarction occurred.

The Q-T type in this group could be classified more often than in the preceding group. A Q_3-type was observed four times, a Q_1-type, three times. In the other five instances the Q-type could not be determined. In four instances the location of the infarct corresponded to the Q-type; in three it did not. In the five in which the Q-type could not be determined, naturally no correlation could be made. A T_3-type occurred in eight instances, in one instance it was not altogether characteristic; a T_1-type occurred three times, but was not

absolutely characteristic in any. In one record the T-type could not be determined. The location of the infarct corresponded to the T-type localization of Barnes and Whitten in four cases; in five it did not. In three instances no correlation could be made. A deep negative Q_3 was found in this series when the infarct was located in the anterior as in the posterior wall of the septum. This does not agree with the conception of Fenichel and Kugel.[37]

Interpretation of the Electrocardiographic Findings.—This study indicates that the electrocardiogram, so far as the standard three leads are concerned, does not always aid in determining whether or not coronary thrombosis or myocardial infarction is present. The electrocardiogram also does not always aid in estimating the age of the infarct. It is, of course, possible that more information might be obtained if more frequent electrocardiograms are taken and the records compared. The advantage of taking records early in middle life to serve as "controls" for subsequent records is obvious. Such "control" records were of considerable value in six instances in this series. The electrocardiographic changes generally assumed to be due to recent myocardial infarcts may also occur in instances of old infarcts or where no infarct is present. These observations suggest that the characteristic electrocardiographic changes supposedly due to recent myocardial infarcts may be produced by some other factor, such as myocardial ischemia brought on by sudden myocardial insufficiency or by sudden reduction in the force necessary to drive blood through the narrowed coronary arteries. In other words, interference with the coronary blood supply in hearts with marked sclerosis and gradual narrowing of the lumina of the coronary arteries may cause changes in the electrocardiogram which are similar to (or nearly similar to) those produced by thrombosis and infarction. Hence the electrocardiogram may be misleading if reliance is placed entirely on it.

This study further shows that so far as single standard lead records (and even occasionally where serial records are available) the electrocardiogram (1) may fail to show changes considered characteristic of recent infarction when an infarct is present; (2) may show changes compatible with infarction when none is present; (3) may show changes characteristic of recent infarction in the presence of an old infarct; (4) may show changes suggestive of an old infarct in the presence of a recent one; and (5) may show changes commonly produced by coronary sclerosis and myocardial fibrosis in the presence of old healed infarcts. Therefore, the electrocardiogram may entirely fail to give any clues as to the full significance of previous clinical attacks.

Furthermore, we believe that it is not feasible to locate the position of the infarct from records obtained with the standard three leads. If it is assumed that the location of the infarct determines electro-

cardiographic types, this study shows that there must be other factors which modify the appearance of the records (cf. Korey and Katz[38]). Perhaps, as Wilson and his associates[32] suggested, the character of the electrocardiogram may depend to some extent on the location of the infarct with reference to the endocardial and epicardial surfaces of the heart. It is also possible that the condition of the myocardium and the position of the heart prior to infarction may play an important rôle (cf. Katz and Ackerman[39]). While it is of interest to attempt to classify the electrocardiograms into various T- and Q-types, one should not become so engrossed in this endeavor as to lose sight of the fact that many records cannot be so classified. It is more important to take serial records at frequent intervals in suspected cases and to examine the records for minor changes, especially in the contour and level of the S-T segment and contour and direction of the T-wave. If this is done, recent coronary thrombosis and myocardial infarction will be overlooked in fewer cases, although the error of diagnosing infarction and thrombosis when they are not present may still occur when the coronary arteries are markedly sclerosed. The recent work of Wolferth and Wood,[40, 41, 35] of Wilson and his associates[32] and of Katz and Kissin[42] indicates that the frequency with which myocardial infarction can be diagnosed is increased by taking a fourth lead from the chest in addition to the standard three leads.

The variability of the electrocardiograms taken when infarcts were not present suggests that the electrocardiographic changes seen in coronary sclerosis are not due to the fibrous replacement of the heart muscle—unless there is serious interference with the conduction pathways—but are expressions of the damage to the apparently normal muscle resulting from a diminished blood supply of the whole heart which the diffuse arteriosclerotic process in the coronary arteries may produce.

DISCUSSION OF CLINICAL FINDINGS

From the clinical standpoint the method of this study has some disadvantages. Thus is may be argued that some of the patients were not sufficiently studied from the cardiac angle. It is, however, unlikely that significant symptoms or signs were overlooked, particularly attacks suggestive of angina pectoris and congestive heart failure. On the other hand, from the clinical standpoint this approach has the distinct advantage of presenting a group of patients which more nearly represents the average likely to be encountered by the profession at large, rather than a group selected by the specialist in internal medicine. As has been seen from the case reports, a large percentage of the patients sought relief from conditions which were primarily surgical, medical or neurological with cardiac symptoms either absent or occupying a minor place.

Incidence and Associated Lesions.—Before reviewing the points bearing directly upon the clinical picture of coronary thrombosis and myocardial infarction, a brief discussion of the incidence and associated lesions is given in Table III.

TABLE III

A. Incidence:

Sex: Males, 28; females, 6.
Age: 45 to 76 years (majority between 61 and 70).

B. Associated lesions:

1. Generalized arteriosclerosis: 34 (moderate, 18; severe, 16).
2. Nephrosclerosis of the arteriolar variety, 9.
3. Hypertension, 13.
4. Pulmonary lesions:

   Infarcts, 9.
   Embolism of pulmonary artery without infarction, 1.
   Bronchopneumonia, 5.
   Abscess, 1.
   Chronic caseous or fibrous tuberculosis, 4.

5. Lesions in the gastrointestinal tract (including the gallbladder and liver):

   Carcinoma, 5.
   Polyposis, 2.
   Intestinal obstruction, 1.
   Diverticulitis, 1.
   Cholelithiasis, 2.
   Cholecystitis, 2.
   Laennec cirrhosis, 1.

6. Infarcts in organs other than the heart or lung, 10.
7. Glandular hyperplasia of the prostate, 6.
8. Encephalomalacia, 4.
9. Diabetes mellitus, 4.

The presence of generalized arteriosclerosis in every patient is not surprising. Only 13 had evidence of hypertension clinically; some cases may, however, have been overlooked. With the exception of infarcts in other organs and possibly carcinomas, the incidence of other than cardiac lesions is about what might be expected in this age group. Associated lesions assume importance in the clinical consideration of coronary disease when they mask or confuse cardiac symptoms, increase the work of the heart, require surgical intervention, or divert the attention from the heart with the result that this organ is not carefully examined.

Pulmonary Lesions.—Bronchopneumonia occurred chiefly as a terminal event. In at least one instance, however, it precipitated the terminal failure. In another instance the symptoms and some of the findings of bronchopneumonia were interpreted as those of coronary thrombosis. Pulmonary infarction was usually secondary to the cardiac mural thrombi, but in at least one instance the symptoms were interpreted as those of coronary thrombosis. In another instance the presence of pulmonary infarction cast doubt on the existence of coro-

nary thrombosis and led to the explanation of the symptoms and findings on the basis of the pulmonary lesion alone (cf. Hamburger and Saphir[43]). It must be borne in mind, however, that pulmonary infarction should lead to the suspicion of the occurrence of recent myocardial infarction unless another cause is demonstrable. Of the nine instances of pulmonary infarction in this study seven resulted from emboli arising from mural thrombi of the right auricle and only two from emboli originating in the right ventricle. In addition there was one instance of a mural thrombus of the right auricle without pulmonary infarction. Pulmonary infarction following myocardial infarction does not necessarily indicate that the myocardial infarct is located in the interventricular septum adjacent to the right ventricular cavity. It may rather indicate myocardial insufficiency, cardiac dilatation, and consequent auricular thrombi.

Abdominal Lesions.—Some of the abdominal lesions in this group of patients were found incidentally at autopsy. Most of them were recognized clinically while the coronary and myocardial disease was overlooked. With one exception they led to surgical intervention. While it is possible in one or two instances that some of the abdominal symptoms were produced by the coronary disease, the cardiac complication in the other instances was overlooked mainly because the coronary occlusion or thrombosis, or myocardial infarction was clinically "silent." It so happens that the error of operating on a patient with coronary thrombosis in the absence of an abdominal lesion was not made in this particular series. The incidence of carcinoma (all of the gastrointestinal tract) is rather high (15 per cent). It is well known today that the pain of coronary thrombosis may appear only in the upper abdomen (Levine and Tranter,[44] Hamburger[45]). This has been emphasized so much that we are in danger of forgetting that an elderly, arteriosclerotic individual can have abdominal pain resulting from an abdominal lesion even though other symptoms might point to the heart. Errors in diagnosis either way are unfortunate and should be studiously avoided.

Infarcts in Other Organs.—In one instance a renal infarct was mis taken for coronary thrombosis; in another a splenic infarct was diagnosed coronary thrombosis. Other instances of infarcts were clinically not misleading. In one instance, however, hemiplegia following cerebral embolism diverted attention from the heart.

Diabetes Mellitus.—Four patients had diabetes mellitus. This incidence is less than some observers report (Levine and Brown,[2] Nathanson[46]). If the patients comprising this series represent, as we believe, the averages which one might encounter, it follows that diabetes mellitus is not so frequently present as may be inferred from the recent literature.

Anesthesia and Surgical Procedures.—It has been stated repeatedly in the individual case reports that anesthesia and surgical procedures play an important rôle in the causation of coronary thrombosis and in precipitating conditions leading directly to death. Spinal anesthesia seems to be particularly contraindicated because of the associated lowering of arterial blood pressure. When surgical intervention is imperative in the presence of coronary occlusion, myocardial infarction, or even advanced coronary arteriosclerosis, a local anesthetic with adrenalin is preferable. If this is not practical, ethylene skillfully administered should be employed. The importance of carefully evaluating the cardiac status of patients upon whom operation is contemplated is emphasized (1) by the fact that severe lesions in the coronary arteries and the myocardium were clinically "silent" in 13 out of the 34 patients, and (2) by the fact that death was precipitated by operative procedures in some of these patients (death being directly referable to the severe coronary lesions or their resultant myocardial changes). Such an evaluation is particularly important in the presence of generalized arteriosclerosis, and must be used to help determine the expediency of surgical intervention. If there is any doubt as to the presence of "silent" coronary lesions or if there is a history of angina pectoris, only emergency operations should be performed and every effort must be made to minimize shock, maintain water balance, aid the coronary circulation, and avoid as far as possible anything which would throw an additional strain upon the heart, not only during the operation but throughout convalescence (Hamburger[47]). It may be mentioned in this connection that gastrointestinal x-ray examinations also carry the similar hazard of sudden death in this type of patient (cf. Case XV) (cf. Hamburger[45]).

CLINICAL PICTURE

The syndrome of "coronary thrombosis" is generally conceived to consist of a sudden attack of severe, agonizing substernal or precordial pain lasting from thirty minutes to several hours and associated with pallor, clammy sweat, faintness and a fall in blood pressure (cf. Herrick,[4] Riesman and Harris[3] and Scott[48]). The pain is unrelieved by nitrites and subsides, if at all, only after large doses of morphine. If to this symptom complex is added the development of fever and leucocytosis, one feels reasonably sure that myocardial infarction had occurred. This impression becomes a certainty if a pericardial friction rub is heard. In comparing the clinical records of the thirty-four patients in this study with the above picture many interesting and some unexpected discrepancies are disclosed.

Nature and Duration of Pain.—Only eighteen patients, or little more than half of the patients, had attacks of pain definitely or reasonably

referable to the heart. In nine of these patients the attacks occurred only after effort (Heberden's angina); in four pain occurred unrelated to effort; the remaining five had both types of pain attacks.

In the group with definite Heberden's angina (fourteen patients altogether) it was impossible to tell in many instances which attacks or which type of pain coincided with coronary thrombosis or myocardial infarction. In three instances (Cases XVIII, XIX and XXVIII) the evidence is reasonably clear that angina of effort developed following the coronary thrombosis or myocardial infarction. The occurrence of pain unrelated to effort has been given as a differential diagnostic point in determining the occurrence of coronary thrombosis. There were only four instances in which an attack of pain unrelated to effort could reasonably be correlated with the occurrence of coronary thrombosis or myocardial infarction. Coronary sclerosis and myocardial fibrosis alone were present in four instances at the time attacks of pain unrelated to effort occurred, showing that in the presence of these lesions obvious exertion is not a prerequisite for the production of pain.

Localization of pain outside the cardiac area was most frequent in the attacks unrelated to effort. In four instances pain was felt solely in the epigastrium, one attack being associated with nausea and vomiting. It has also been said that epigastric localization of pain favors the diagnosis of coronary thrombosis. Of five attacks of pain unrelated to effort and with epigastric localization, three did not signalize coronary thrombosis. In the group with Heberden's angina (fourteen patients altogether) pain occurred in the epigastrium in one instance and in the face and neck in another in addition to being substernal.

In two instances correlation between the attacks of pain and the anatomical findings was not possible because of multiplicity of lesions.

In addition to the eighteen patients discussed above, three other patients had attacks of epigastric or abdominal pain not related to effort and which could not be ascribed definitely to cardiac lesions. In one of these patients (Case VIII) old coronary sclerosis or occlusions might have caused the attacks of epigastric pain, although an infarct of the spleen was also present. In the second (Case XV) there was abdominal pain about the time of coronary thrombosis, but the patient also had carcinoma of the stomach. In the third (Case XVII) an attack of right upper quadrant pain was possibly caused by coronary thrombosis but clinically was more typical of gallbladder disease.

Duration of pain is not a reliable differential diagnostic point in determining the occurrence of coronary thrombosis because of the frequent occurrence of attacks of pain lasting for hours which did not signalize coronary thrombosis. There are no clear-cut instances in our series of short attacks of pain signalizing coronary thrombosis or myocardial infarction.

Severity of pain also is not a reliable guide in the differential diagnosis of coronary thrombosis, since there were attacks of pain, unrelieved by nitrites or morphine, not associated with the occurrence of coronary thrombosis. On the other hand, some comparatively mild attacks of pain signalized coronary thrombosis. Some of the variability in the severity of pain encountered may be explained, in part at least, by variability in the sensitivity of the individual to painful stimuli, a subject which has been emphasized recently by Libman[49] who divides patients into hypo- and hypersensitive groups.

It is interesting to note that thirteen patients did not give a history of any cardiac pain. This group constitutes 38 per cent of the total number of patients in this study and includes those with various types of anatomical lesions, namely, recent coronary thrombosis without myocardial infarction—2 instances, recent coronary thrombosis with myocardial infarction—4, recent myocardial infarction without coronary thrombosis—2, old sclerotic coronary occlusion—1, old coronary thrombosis—1, old coronary thrombosis with myocardial infarction—2, and old myocardial infarction without coronary thrombosis—3. Some hearts had lesions which developed at different times, accounting for the overlapping (Cases XVI, XXXI, XXXII, XXXIII). Every one of these thirteen hearts, however, showed coronary sclerosis and myocardial fibrosis. Congestive heart failure, debilitating disease, or clouded sensorium may explain the absence of pain in a few of these thirteen patients but not in the majority. It may be emphasized that some of these "silent coronary accidents" occurred while the patients were under daily observation in the hospital.

Other Signs and Symptoms.—In looking for other possible clinical signs of coronary thrombosis or myocardial infarction in the group of patients without pain, it was noted that five had an attack of sudden dyspnea related to the development of coronary thrombosis. These sudden attacks of dyspnea were not always accompanied by pallor, fall in arterial blood pressure, fever and leucocytosis. It seems justifiable, therefore, to emphasize the fact that sudden dyspnea may be the only clinical sign of coronary thrombosis. In one instance in the group of patients without pain an attack of faintness was apparently the only significant sign of coronary thrombosis.

Aside from pain and sudden dyspnea, the following summary may be given concerning the remaining symptoms and signs considered characteristic of coronary thrombosis and myocardial infarction. Myocardial infarction was usually associated with fever, although in three instances it was not. In every instance of recent infarction in which a white blood cell count was made, a leucocytosis was found. When previous blood pressure readings were available as controls, a fall in arterial pressure coinciding with coronary thrombosis was usually

noted. But in at least four patients (Cases II, VII, XI and XXVI), the arterial pressure was well maintained or actually rose. Recent or organizing pericarditis occurred nine times, and in four of these instances a friction rub was heard. The friction rub does not indicate that the infarct is located anteriorly, since in two of these four the infarct was found in the posterior wall of the left ventricle. The pulse was usually rapid and of poor quality. Hyperpnea of varying degrees and occasionally dyspnea occurred immediately following coronary thrombosis whether pain was present or not. Pallor, sweating, and weakness were inconstant.

In view of all the facts presented in this discussion it appears impossible in the present status of our knowledge to differentiate clinically between myocardial infarction brought about by coronary thrombosis and that following arteriosclerotic narrowing or occlusion of the coronary arteries. This study also emphasizes the great difficulty of determining clinically the occurrence of coronary thrombosis and myocardial infarction, either because the thrombosis and infarct may occur "silently" or because the characteristic picture may be found in the absence of thrombosis and infarction.

SUMMARY AND CONCLUSIONS

The material of this study comprises thirty-four cases selected by the pathologist on the basis of the anatomical lesions, without previous knowledge of the clinical and electrocardiographic findings. After the anatomical material had been studied, the clinical and electrocardiographic records were reviewed, and the attempt was made to correlate these findings with the anatomical lesions.

Both coronary arteries were involved in all hearts examined. The more severe lesions were found in the left coronary artery, especially in the descending branch. Whenever a myocardial infarct was encountered, at least two branches of the coronary arteries supplying the infarcted areas were involved. The infarcted areas in general were present in the regions supplied by the diseased coronary arteries. Occasionally, a recent thrombus was found in one coronary artery, while the recent infarct was located in an area supplied by the previously occluded opposite coronary artery. Apparently the infarcted area, prior to infarction, was supplied by collateral anastomoses. In four hearts, infarcts were present without any occlusion of the coronary arteries, although their lumina were markedly narrowed. Such infarcts were probably caused by transient myocardial insufficiency, which in the presence of narrowed coronary arteries led to a temporarily inadequate blood flow. Some degree of myocardial fibrosis was present in all hearts.

Patients with myocardial infarcts may die suddenly or succumb slowly. In some instances the final factors, which led to a sudden

greater demand upon the heart just before death, could be deduced. In the great majority of patients, death ensued because of myocardial incompetence associated with myocardial infarction. Sudden death following the occlusion of a single main branch of the coronary arteries was not encountered. Three patients dying suddenly showed recent thrombi in a main branch of one coronary artery, the opposite artery showing an old occlusion.

As far as single standard lead records are concerned (and even occasionally where serial records are available) the electrocardiogram may fail to give any clue as to the full significance of previous clinical attacks. It does not always aid in determining whether or not coronary thrombosis or myocardial infarction is present. The electrocardiographic changes supposedly characteristic of recent myocardial infarcts may be caused by some other factor such as myocardial ischemia brought about by sudden myocardial insufficiency or by sudden reduction in the force necessary to drive blood through the narrowed coronary arteries.

The attempt to locate the position of the infarct from records obtained with the standard three leads is not feasible. If it is assumed that the location of the infarct determines electrocardiographic types, this study shows that there must be other factors which modify the contour of the electrocardiograms.

The variability of the electrocardiograms taken when infarction was not present suggests that the changes seen in coronary sclerosis and myocardial fibrosis are not due to the fibrous replacement—unless there is serious interference with the conduction pathways—but are evidence of damage to the intact myocardium accompanying the lessened blood supply through the arteriosclerotic coronary arteries.

Pain definitely or reasonably referable to the heart occurred in 18 of the 34 patients. There were only four instances in which an attack of pain unrelated to effort could reasonably be correlated with the occurrence of coronary thrombosis or myocardial infarction, yet coronary thrombosis was encountered 32 times. On the other hand, coronary sclerosis and myocardial fibrosis alone were present in four instances at the time attacks of pain unrelated to obvious effort occurred. The duration and severity of pain were found to be unreliable guides in diagnosing coronary thrombosis and myocardial infarction.

Thirteen of these 34 patients did not give any history of cardiac pain. Congestive heart failure, debilitating disease, or clouded sensorium may explain the absence of pain in a few of these patients but not in the majority. Some of the so-called "silent" coronary accidents occurred while the patients were in the hospital. Sudden dyspnea may be the only clinical sign of coronary thrombosis.

Myocardial infarction was usually associated with fever, although in three instances it was not. In every instance of recent infarction in which a white blood cell count was made, leucocytosis was found. When previous blood pressure readings were available as controls, a fall in arterial pressure coinciding with coronary thrombosis was usually noted; but in at least four patients the arterial pressure was well maintained or actually rose. Recent or organizing pericarditis occurred nine times, but a friction rub was heard in only four instances. The friction rub does not indicate that the infarct is located anteriorly, since in two of these four the infarct was found in the posterior ventricular wall. The pulse was usually rapid and of poor quality. Hyperpnea of varying degrees, occasionally dyspnea, occurred immediately following coronary thrombosis whether or not pain was present. Pallor, sweating, and weakness were inconstant signs.

Pulmonary infarction following myocardial infarction may be due to emboli from mural thrombi of the right auricle or right ventricle. The incidence of carcinoma of the gastrointestinal tract was rather high (15 per cent). Diabetes mellitus in our series was not so frequently present as might be inferred from the recent literature. The fact that the pain of coronary thrombosis may appear only in the upper abdomen has been emphasized so much that there is danger of overlooking abdominal lesions.

Anesthesia and surgical procedures may precipitate coronary thrombosis or conditions leading directly to death. The cardiac status of patients in the fourth decade or later, upon whom operation is contemplated, should therefore be carefully evaluated.

Not coronary thrombosis nor myocardial infarction nor coronary arteriosclerotic occlusion can be the anatomical equivalent of angina pectoris because these lesions were found not only in the presence of angina pectoris but also in patients who never had attacks of angina pectoris. Besides, these lesions were not constantly present in hearts of patients dying following attacks of angina pectoris. Only one anatomical change was common to all hearts of patients who had attacks of angina pectoris, namely, coronary sclerosis and myocardial fibrosis. To the morphologist, coronary sclerosis and fibrosis of the heart mean a labile myocardium which may fail suddenly. It seems that the sudden failure, or the subsequent events, is intricately linked with anginal attack in some manner as yet undetermined.

In the present state of our knowledge, it appears impossible to differentiate clinically between myocardial infarction brought about by coronary thrombosis and that following arteriosclerotic narrowing or occlusion of the coronary arteries. It is also difficult to determine the occurrence of coronary thrombosis and myocardial infarction clini-

cally, either because the thrombosis and infarct may occur "silently," or because the characteristic picture may be found in the absence of thrombosis and infarction.

We are indebted to the staff of Michael Reese Hospital for the privilege of studying the clinical records of some of these patients.

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THE HEART IN TYPHOID FEVER

A Clinical Study of 30 Patients*

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OPPORTUNITIES for studying the cardiovascular system during the course of typhoid fever have been greatly lessened during recent years, so that little data based upon modern concepts of circulatory disease have been accumulated.

The most comprehensive study is that made by Brow[1] during an epidemic of typhoid fever in 1929. He studied sixty-five patients and found that 21.5 per cent showed abnormal electrocardiograms at some periods of the disease. Prolongation of the P-R interval was found in fourteen cases varying in extent from 0.21 sec. to 0.28 sec. The earliest change was noted on the eleventh day and the latest upon the forty-third day of the disease. Only two patients showed T-wave changes. A careful physical examination of the heart during the course of the disease failed to show any evidence indicating heart failure or involvement of the myocardium.

From 1923 to 1933, inclusive, 175 patients ill of typhoid fever have been treated on our medical service. During the past four years we have selected thirty for special cardiovascular studies. Of these, twenty-nine gave no history or physical evidence of previous circulatory disease, and one patient with a history of two attacks of rheumatic fever had the physical phenomena of mitral stenosis.

The routine adopted during this study consisted of daily blood pressure estimations, electrocardiograms once a week, with repetition every third day if changes were found, a daily clinical study of the cardiovascular system, noting particularly phenomena indicative of heart failure of the congestive type, arrhythmias, murmurs, quality of the first cardiac sound, and cardiac size.

The treatment emphasized a high caloric diet, allowing 60 calories per kilogram of body weight. Its composition was protein, 2 gm.; carbohydrates, 5 gm.; and at least 50 c.c. of fluids per kilogram of body weight. No drugs were prescribed except simple remedies to control delirium, cough, diarrhea, and restlessness. No remedies which affect the heart or vascular system were prescribed.

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TABLE I

THE SIGNIFICANT ELECTROCARDIOGRAPHIC DEVIATIONS FROM THE NORMAL FOUND AMONG THE THIRTY PATIENTS STUDIED

CASE	AGE	PULSE RATE*	AVERAGE BLOOD PRESSURE†	ELECTROCARDIOGRAM			REMARKS
1. H. M.	16	79	104/54	P-R	interval 0.21 sec.	25th day	Recovery
2. K. J.	15	88	112/68	P-R	interval 0.23 sec.	24th day	Recovery
3. P. C.	18	87	102/48	T inverted	Lead I	23rd day	Recovery
4. D. C.	20	94	118/59	P-R	interval 0.26 sec.	27th day	Recovery
5. J. R.	17	107	94/54	P-R	interval 0.24 sec.	15th day	Recovery
6. S. H.	19	106	102/62	P-R	interval 0.26 sec.	13th day	Recovery
7. K. G.	17	100	112/74	T isoelectric	Lead I		
				T inverted	Lead II, III	44th day	Recovery
8. F. B.	27	88	102/57	P-R	interval 0.28 sec.	12th day	Recovery
9. L. S.	40	116	100/64	P-R	interval 0.22 sec.	21st day	Death
							Perforation
10. G. P.	19	71	101/62	P-R	interval 0.24 sec.	28th day	Recovery
11. E. R.	32	107	118/55	T inverted	Lead II, III	31st day	Recovery
							Relapse
12. C. H.	21	100	104/52	T inverted	Lead I, II	15th day	Recovery
13. L. J.	30	115	94/46	T diphasic	Lead I, II		
				QRS slurred	interval 0.12 sec.	9th day	Recovery
14. E. F.	24	105	98/47	P-R	interval 0.26 sec.	18th day	Recovery

*Rate recorded with first abnormal electrocardiogram.

†The average systolic and diastolic pressures from daily records.

Table I gives a summary of the pulse rate, average blood pressure, and the significant electrocardiographic deviations from the normal in those patients showing abnormal electrocardiograms.

DISCUSSION

Electrocardiograms.—Forty-six per cent of the patients showed significant changes in the electrocardiogram. The earliest change noted was on the ninth day, and the latest on the forty-fourth day. It is significant that the disturbances observed in the electrocardiograms continued in most instances for a brief period, lasting in only two instances longer than six days. In every patient the electrocardiograms eventually became normal. In not a single patient was there any disturbance of cardiac rhythm except a moderate degree of sinus arrhythmia observed in an occasional patient during convalescence.

Lewis[2] states that conduction defects occur only in the severe types of infection. In our series there was no noticeable difference in the frequency of electrocardiographic changes in those with clinically severe infections and in those with mild infections.

Chagras[3] observed that inversion and diphasic T-waves were the most frequent alteration in the electrocardiograms.

Our findings are in accord with those of Hyman[4] and of Brow, who both noted prolongation of the P-R interval as the most frequent disturbance of cardiac mechanism.

Cardiac Murmurs.—One patient on admission had the physical phenomena of mitral stenosis. He gave a definite history of two attacks of rheumatic fever, at the ages of fourteen and nineteen years. No additional changes were noted in the physical phenomena or electrocardiograms during the course of a very severe typhoid infection. Only two other patients showed murmurs during the course of their illness. These two patients had repeated intestinal hemorrhage with the consequent development of severe grades of secondary anemia. The murmurs were systolic in time, heard both at the apex and over the base of the heart. At the time the murmurs were heard, the hemoglobin was 46 per cent in one patient and 39 per cent in the other. Following transfusions with a partial relief of anemia, the murmurs disappeared. No endocardial or pericardial murmurs were heard in any of the patients, indicating that neither pericarditis nor endocarditis developed to a degree sufficiently significant to produce the usual phenomena of these conditions.

Heart Size.—Special effort was made to determine whether cardiac dilatation occurred during the course of typhoid fever. Reliance was placed principally on the position and character of cardiac apex in determining heart size; nevertheless, in ten of the patients seven-foot x-ray plates were used. In only one patient was there any evidence of conclusive character indicating that cardiac dilatation had occurred. In

this patient, in whom repeated intestinal hemorrhage occurred, there was an excursion of 1.5 cm. of the left border of the heart to the left. In none of the remaining twenty-nine patients could there be demonstrated phenomena indicating that there was a material change in the size of the heart. This statement is applicable both to those who showed changes in the electrocardiograms and to those who had normal electrocardiograms.

Heart Sounds.—The first heart sounds in typhoid fever are notably weak in quality. Frequently in this study the heart sounds were recorded as being short in duration and muffled or distant in quality. While this phenomenon is observed in practically all patients during the active stage of typhoid fever, its significance is difficult of interpretation. It might be interpreted as meaning that heart muscle pathology existed, yet this supposition was not substantiated by cardinal phenomena of congestive heart failure, and a gallop rhythm was never observed. The second sounds were not significantly altered except in two patients. In these two it was noted that the intensity of the second pulmonic sound was increased.

Blood Pressure.—As has been previously observed the blood pressure has been relatively low in all of the patients studied. This is true of both the systolic and diastolic pressures. After the occurrence of intestinal hemorrhage, there frequently follows a critical fall in both the systolic and diastolic blood pressures. This is a more sensitive index of the occurrence of hemorrhage than the rectal temperature, for we have frequently observed blood pressure changes with no significant temperature alterations.

Heart Failure.—In a review of 175 patients who had typhoid fever, thirty of whom are included in this study, not a single patient has shown the phenomena characteristic of congestive heart failure. This is significant for Marris[5] observed high venous pressures in typhoid patients. In none of the patients in this series was there clinical or instrumental evidence of general venous hypertension. Occasionally moderate distention of the veins of the neck occurs in those patients who have marked degrees of tympanitis, yet the venous distention disappears with relief of abdominal distention.

Pulmonary edema associated with left ventricular failure did not occur in a single patient except as a terminal event in those who were dying from complications, such as typhoid perforation. It would be reasonable to expect ventricular failure in patients in whom toxic degeneration of the heart muscle is apparently a rather common complication; yet, from a study of this series, it appears as if an inhibiting factor prevented such serious disturbances of heart muscle function.

SUMMARY AND CONCLUSIONS

1. Of the thirty patients, 46.6 per cent showed significant changes in the electrocardiograms, although the changes were transient in nature.

The fact that evidences of cardiac dilatation and heart failure were strikingly absent suggests that the pathological changes which were responsible for the electrocardiographic alterations were either mild in degree or were localized.

2. No disturbances of rhythm occurred; a gallop rhythm was not observed; and there was a notable absence of the phenomena of congestive failure.

3. From a clinical viewpoint the heart presents no significant problem in the treatment of typhoid fever.

4. A study of the literature dealing with typhoid fever prior to the use of high caloric diets indicates that the toxemia of the disease was much greater and serious cardiovascular complications were common. Comparing the recent studies of Brow and the studies herein reported with former studies,[6] one ventures the conclusion that the reduction in the serious circulatory complications may be attributed to the character of the diet now employed in the care of typhoid patients.

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ON THE USE OF CHEST LEADS IN CLINICAL ELECTROCARDIOGRAPHY

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SINCE the introduction of Lead IV by Wolferth and Wood in January, 1932,[1] the use of chest leads has become popular as a routine procedure in clinical electrocardiography. It has stimulated an interest which led cardiographers and clinicians to make further search for leads that might disclose evidences of myocardial damage not readily discernible in the standard leads originally adopted by Einthoven. Consequently various combinations of chest electrodes, or combinations of one chest and one limb electrode, have been employed to "improve" on Lead IV. Some have advocated multiple combinations or hook-ups, advancing the contention that when Lead IV fails, some other chest lead of the group may serve. Nevertheless, up to date, Lead IV still holds sway.

By this lead is meant a combination of two chest electrodes, one anterior and one posterior. The right arm electrode is applied to the immediate vicinity of the cardiac apex, and the left arm electrode* is applied to the dorsum—slightly above and slightly medial to the angle of the left scapula. Tracings derived by this lead, it has been claimed, disclose evidences of myocardial involvement at times when they are not readily seen in the standard leads. For the normal tracing recorded by this lead, Wolferth and Wood presented criteria essentially as follows: The P-wave is negative and small; the QRS is large, diphasic, and its initial deflection is negative; the T-wave is large, negative and is preceded by only a very short isoelectric period. The outstanding feature of this tracing is a magnification of the entire ventricular complex with an inversion of its principal components.

Obviously then, abnormalities in Lead IV are manifested by alterations in the ventricular complex. A shallow or upright T-wave or an absence of the initial negative deflection in the QRS complex would constitute abnormalities in Lead IV. A deviation of the RS-T segment in Lead IV has the same clinical significance as in the standard leads.

To Lead IV, Wolferth and Wood soon added Leads V and VI. This simply meant additional combinations between the two chest electrodes mentioned and the left foot; Lead V recording the potential difference between the *apex* electrode and *left foot;* and Lead VI, the potential difference between the *dorsal* electrode and *left foot.* For reasons to be

*Right arm electrode and left arm electrode refer to electrodes situated anywhere on the body surface, so long as they are attached to lead cables which in standard electrocardiography are connected with the right arm and left arm respectively. For brevity, such electrodes will be designated in this article merely as the R and L electrode.

explained later, Lead V is essentially of the same configuration as Lead IV, and in the light of our present knowledge Lead VI is of no particular value because it yields small deflections, generally smaller than any of the standard leads.

The presentation of Lead IV as an aid in clinical electrocardiography came to us at a time when it was felt by many that the use of the electrocardiogram had nearly reached the height of its potentiality as a diagnostic aid. It came at a time when we were much puzzled by minor changes in the ventricular portion of the electrocardiogram. The prospect of solving them seemed remote, and this, in spite of our having entered the fourth decade of electrocardiography.

The normal electrocardiogram had been deciphered in great detail by the old masters over thirty years ago. Common deviations from normal, as found in disorders of cardiac rate and rhythm, have been presented repeatedly, and their meaning has been clarified. Abnormalities in the auricular P-wave indicating anatomical or physiological changes in the auricles have become common knowledge. Some twenty years ago certain changes in the initial ventricular complex (QRS) had been described, leading to inferences as to types of defect in intraventricular conduction. About ten years ago we had added valuable information as to the meaning of gross changes in the terminal portion of the ventricular complex (R-T and T) in estimating the degree and locating the site of damage in the ventricular myocardium, due to coronary occlusion. Subsequently our knowledge was extended to include the meaning of similar R-T and T changes in other conditions producing localized impairment in myocardial function, as in the pericarditides, inflammatory, neoplastic, and traumatic lesions of the myocardium. The names of the workers who have made these valuable contributions, decade by decade, need not be mentioned here. They are recorded in all modern texts dealing with the elements of electrocardiography.

In the foregoing it has been our object to emphasize, in an approximately chronological order, the gradual, slow rate of accumulation and the subsequent sum total of our knowledge in electrocardiography when Lead IV was introduced. In this connection it should be stressed that when this special lead was introduced, we were preoccupied principally with the study of T-waves and R-T changes as possible indications of myocardial damage and that in the study of these we have been able to interpret the meaning of gross changes only. Minor variations in the terminal phase of the electrocardiogram have been meaningless and are, in a measure, meaningless today. Experiments on hearts of animals have not been productive of information beyond the localization of gross lesions, "anterior" or "posterior" surface lesions. Electrocardiography was in a state of apparent standstill or, at best, at a stage of very slow progress. It was at this time that Lead IV was offered as a further means of information, and, naturally, the subject was received with a

great deal of enthusiasm. The literature that followed with intentions to confirm and presumably to elaborate on the usefulness of Lead IV, reflected this enthusiasm unmistakably. Some of the earlier literature seems to have been colored by it as if expressing a wish that chest leads would do what the standard leads could not do.

Several articles appeared in the literature in rapid succession, confirming the "criteria" for Lead IV, and endorsing its adoption as a part of routine electrocardiography. These articles appeared at a time when the originators of Lead IV seemingly had not as yet crystallized their own ideas as to the value of chest leads as a clinical routine. They were still in the early experimental stage of their work. As their subsequent articles will show, they advanced cautiously and came to their conclusions only after long and painstaking experimental studies. The literature will be reviewed in sufficient detail to bring out some of these points.

The present popularity of chest leads as a routine electrocardiographic procedure, coming almost immediately in the wake of the introduction of Lead IV, and the type of literature and investigations which the introduction of this special lead has prompted warrant at this time a critical review of the literature as well as a careful examination of the rôle of chest leads in general, and of Lead IV in particular, as aids in clinical electrocardiography. Such an examination at this time may lead to a clearer understanding of the investigations which the introduction of Lead IV has prompted in the past and may point out the directions in which it further tends to stimulate the study of electrocardiography.

In reviewing the early literature, one gains the unavoidable impression that, in the enthusiasm attending the introduction of Lead IV, articles dealing with the subject have, perhaps inadvertently, underrated abnormal findings in the standard leads in cases used to illustrate the diagnostic advantages of chest lead tracings and that they have correspondingly overemphasized the relative diagnostic value of abnormal chest lead findings. Such overemphasis has been exemplified in the literature by the use of terms, such as "specific" and "pathognomonic," in describing tracings derived by Lead IV, while obviously abnormal standard lead tracings are often characterized as having "no diagnostic value." These statements will be strengthened by direct references to, and quotations from, leading early articles on the subject.

Although some of the comments accompanying the review of the literature may seem unduly critical, it should be understood at the outset that there is no intention to underestimate the value of contributions presented by pioneers in this field. It is recognized that the work of some, Wolferth and Wood in particular, has been in a measure inspiring and unquestionably stimulating. It is precisely because of this, that a critical review seems timely. It is hoped that such a review at this time may tend to prevent publications based on limited experience and meager information from creating impressions about the value of chest leads

which the originators of this work probably never intended to create. There is also this to be considered. Minor changes in the ventricular complexes of the standard leads, though imperfectly understood today, may prove to have a very significant meaning; but, if as a result of our enthusiastic preoccupation with chest leads we cultivate the tendency to underrate minor changes in standard leads, electrocardiography may suffer a setback. And it may be stated safely that no particular chest lead or leads will displace the standard electrocardiogram, perhaps not even in the study of localized myocardial damage. Standard electrocardiography is built on a firm foundation. It is the creation of a master mind. Its three components are not only distinctive and individually informative, but they have the additional advantage of being interrelated with an almost mathematical precision, leading to wide information on cardiodynamics, beyond the province of chest leads. Furthermore, as pointed out by Wilson, the standard curves are comparatively unaltered by shifting of the electrodes. They remain constant and reliable in form. This is not true of chest leads.*

This brief digression into the properties of the standard electrocardiogram and the implied caution that minor changes be not considered as having "no diagnostic value" will appear more significant as we enter upon the review of the literature.

In their original article Wolferth and Wood[1] report two cases with clinical evidences of coronary occlusion. They state that Lead IV showed "unmistakable deviation" while the standard leads "yielded little or no diagnostic information," except on the fourth day. Actually, perusal of their graphs reveals that the standard leads were also definitely abnormal. The first case, to be sure, showed only a shallow T_1, which in the course of four days took on the form of a high take-off. However, in their second case the standard leads showed not only a shallow T_1 but also a definitely elevated RS-T segment. Furthermore, the standard electrocardiograms in both cases showed progressive changes from day to day. This we know to be strong presumptive evidence of myocardial damage. The authors stress this important point also.

In their next publication,[2] these investigators promptly caution against laying undue emphasis on the importance of Lead IV. They conclude that "the purpose of the paper is to show that Lead IV does not in any way replace the routine electrocardiogram but should be used as an adjunct to it."

Some of the other writers, however, had apparently failed to heed this timely warning. At any rate, they seemingly did not examine their standard leads critically and had almost uniformly conveyed the impression that it is the chest lead which serves as the ultimate criterion in

*Wilson[17] pointed out that shifting the limb electrodes over different parts of the extremities, with the galvanometer string at normal sensitivity, does not appreciably alter the standard electrocardiogram, provided the electrodes remained on the limb. However, if one electrode is transferred to the trunk, definite changes are noted. These become more and more pronounced as the electrode approaches the region of the heart.

the diagnosis of myocardial involvement. The several case reports which followed in the wake of these two publications clearly show an overemphasis of the diagnostic value of chest leads, while they generally refer to the standard leads accompanying them as showing "inconclusive changes."

One of these reports[3] refers to two cases of coronary occlusion. The first case is that of a man forty-four years old with previous hypertensive heart disease and a history of *status anginosus* four days before admission. Three electrocardiograms were taken, one week apart. In this case the standard leads show definite changes indicative of myocardial damage while the chest lead shows only a corresponding T-wave abnormality. Yet, the authors make the startling statement that the "tracings show a pathognomonic R-T anomaly in the chest lead at the time that the conventional leads show only inconclusive changes." Actually the chest lead shows only a diphasic T_4 and a very slight depression of $(R\text{-}T)_4$, approximately 2 mm. As their second case, these authors present an electrocardiogram consisting of four leads taken about six months after a coronary episode. Lead IV shows an upright T-wave. The authors present this case as an evidence of the persistence of a "chest lead anomaly six months after a coronary occlusion." No mention is made of the fact that T_1 of the standard leads in this case also shows a conspicuous inversion (patient had no hypertension). The upright T_4 is obviously the usual counterpart of an inverted T_1. This article clearly overemphasizes the diagnostic importance of the chest lead while it definitely underrates the value of the standard leads.

Another report[4] refers to three cases. The first of these cases is irrelevant. The patient had three successive seizures of angina pectoris. He died during the last attack. Standard leads were taken after the first seizure. They were not significant. No chest leads were taken. The case is recorded in a tone of implied regret, expressing the assumption that if Lead IV had been taken, myocardial damage might have been disclosed. The second case is presented merely as an example of an abnormal Lead IV. In this case the standard leads are also definitely abnormal and are suggestive of a left coronary occlusion (T_1 type). The third case is important in that a diagnosis of coronary occlusion is made on Lead IV alone. This is a case of a thirty-nine-year-old man who had given a history of an occasional substernal pain "on bending over or picking up heavy objects." One day, while at rest, he became dizzy and developed continuous precordial pain, lasting fifteen hours. The pain was not intense; it was "bearable." He received morphine to relieve his "nagging" pain. Physical findings were negative. Electrocardiographic standard leads were normal. With reference to the chest lead the writer states that "Lead IV was characterized by a depressed S-T interval and an inverted T-wave." The case report concludes: "This, with the clinical history justified the diagnosis of a coronary occlusion,

in spite of the meager physical findings." The depression of $(S\text{-}T)_4$ referred to was less than 2 mm., and the negative T-wave in the chest lead was obviously not abnormal. (Case 3, Fig. 4, pp. 422, 423 of publication cited in reference 4.) This case report is discussed at length because it is an example of overestimating the meaning of Lead IV. The clinical diagnosis in this case may have been correct, but the chest lead certainly was not the determining factor in the diagnosis as the conclusion implies. This is clearly an example of overemphasis, definitely not in accordance with the intentions of the original investigators who introduced Lead IV, as subsequent reference to their work will show.

Liberson and Liberson[5] report a series of 75 cases of which 20 were normal, 50 "cardiac suspects," and 5 "coronaries." They have modified the technic of Wolferth and Wood in that they placed the L electrode anteriorly and the R electrode posteriorly, presumably with the purpose of having the main deflection of the chest lead follow the direction of similar deflections in the standard leads. They established criteria for the normal chest lead which were essentially the same as those of Wolferth and Wood, except that in their modified chest lead the main deflections have opposite directions. In their "Lead IV," naturally, the initial ventricular complex has a conspicuous S-wave instead of the Q-wave, and the T-wave is upright. (Wolferth and Wood in their original paper stated that this arrangement of the electrodes was optional.)

These writers report an illustrative case to show that the chest lead may point to a diagnosis of coronary occlusion, "where neither the clinical picture nor the standard leads suggest it." It is true that the chest lead in this case showed a conspicuous deviation of the RS-T segment, suggestive of an acute myocardial involvement; yet, the clinical picture and standard leads taken at this time were also highly suggestive. The patient complained of an "upset stomach" and had a fall in blood pressure from 170/90 to 120/66. Furthermore, the standard leads showed diphasic T-waves in Leads I and II with definite "coving" of their first portion.

The authors state, furthermore, that in this case the S-T changes noted in the chest lead occurred "fully three weeks *before* similar changes in the standard leads" [italics mine]. This is apparently an erroneous conclusion, based on an imperfect appraisal of the clinical history. According to their records, the patient in question left the hospital after his first attack, "improved." He was readmitted fourteen days after the first tracing had been taken, because of an attack of abdominal and chest pain associated with dyspnea. On readmission, he was "acutely ill" and had a thready pulse, temperature, and leucocytosis. Electrocardiograms taken five days later showed marked S-T changes, but this time the changes appeared in Leads II and III of his standard electrocardiogram. The chest lead showed only a shallow T-wave, and no S-T deviation. This patient apparently had a fresh myocardial insult (a pos-

terior wall injury) revealed this time by the standard leads only and the changes in the standard leads were *not,* as the authors indicate, "the appearance of changes at a later date—three weeks later."

In a study of Lead IV, Katz and Kissin[6] examined a group of normal individuals and some with myocardial disease, including eleven who had recent coronary closure. On comparing Lead IV with standard leads in the same patients, they grouped their cases as follows: (1) those with characteristic changes in Lead IV and the standard leads; (2) those with characteristic changes in the standard leads only; and (3) those with characteristic changes in Lead IV only. Their standard lead tracings in subgroup (3) though not "characteristic," are nevertheless abnormal (Fig. 3c, 4a, 4b, 4c in the article cited in reference 6). At any rate, in a strict sense, the group does not show changes in "Lead IV only."

They add their eleven cases to the five previously reported by Wolferth and Wood and state that seven out of this group of sixteen cases "show specific changes in Lead IV only." The changes in the standard leads accompanying Lead IV in this group are not conspicuous, to be sure; yet these tracings show definite abnormalities, sufficient to indicate myocardial involvement. At any rate, the changes in this group are not confined to Lead IV only. Furthermore, the designation of the cardiographic changes in Lead IV as being "specific" is open to objection. The validity of such a designation would depend essentially on the interpretation of the tracing in the light of a clinical syndrome. As a diagnostic criterion in structural heart disease no electrocardiogram per se may be termed specific. The instrument essentially records physiological events. It depicts anatomical changes by inference only. As further evidence that the term "specific" is not a suitable designation for abnormalities in tracings derived by Lead IV or, for that matter by any lead, these writers themselves add in their summary that "the presence of any abnormalities in Lead IV are to be considered in the same way as abnormalities in the ordinary lead. . . . They are less significant when they occur alone than when they are accompanied by other electrocardiographic evidence pointing in the same direction." In the light of these statements then, may it not be asked, "Wherein are they specific?"

Hoffman and Delong[7] reported a study of chest leads of 125 normal cases and a small series of pathological cases. These writers emphasize an important point worthy of special note, namely, that there are changes in the chest lead tracings on slight change in the position of the anterior electrode.

Their pathological cases they group as follows: (1) those showing normal standard leads and abnormal chest leads; (2) those showing abnormal standard leads and abnormal chest leads; and (3) those showing abnormal standard leads and normal chest leads.

In their first group designated as showing normal standard and abnormal chest leads, careful examination of the tracings clearly reveals minor variations in the standard leads (shallow T_1 and T_2, slight inversion of T_1, low voltage QRS, and shallow diphasic T_1 T_2). These changes are sufficient to stamp these standard leads abnormal. In fact, they are suggestive of anterior lesions in those patients who have had a coronary episode. In their third group in which the standards were abnormal and the chest normal, the standard leads show conspicuous changes of the T_2 and T_3 type. This group exemplifies the limitation of chest leads and the indispensability of standard leads.

These workers confirm the important observation of Wolferth and Wood, that at times changes in the chest lead do appear before they are conspicuous in the standard leads. This is a valuable property of chest leads when present. But these workers add, what seems equally important, that frequently chest leads revert to normal before the standard leads. The importance of this lies in the fact that it lends emphasis to the interdependence of chest leads and standard leads. Where one fails, the other may aid. They observed also that in a few instances the chest lead remained abnormal for many months after the standards became normal. This is interesting, but the question may be raised as to what criteria have been used in the evaluation of the standard leads. From the literature reviewed thus far it appears that, while we are busily preoccupied with establishing criteria for chest leads, we seemingly have not as yet agreed on uniform criteria as to what constitutes a normal standard electrocardiogram. When standard lead tracings are properly evaluated, it is found that they, too, remain abnormal for many months, at times even for years.

Goldbloom[8] reports 25 normal cases and a group of 40 ambulatory cardiac cases. Out of the latter group, 13 were previously observed and treated for coronary artery disease with thrombosis. In his studies the writer had used anteroposterior as well as posteroanterior chest leads. He concludes that 30 per cent of his cases of coronary thrombosis show an abnormal Lead IV, "whereas the routine three leads are negative." This conclusion is based on 13 cases of which 4 cases constitute the 30 per cent. The writer presents a table of relative "evaluation" of the four leads in this group (p. 496 of publication cited in reference 8); but the table actually fails to show normal standard leads in the four cases mentioned as constituting the 30 per cent. Two of these cases show abnormal T-waves in two out of the three standard leads. The third case shows a negative T_2 (the T-wave must therefore be negative in one other lead). The fourth case has a diphasic T_3 (here, Lead I must also be diphasic, if the galvanometer string is of the same standard tension in both leads). In a measure, the writer is justified in his conclusion, if regarded in the light of the criteria he sets for his standard leads. For an abnormal standard electrocardiogram to be indicative of

myocardial damage, he requires a "high take-off of the T-wave" or "diphasic T-waves in more than one lead." On the other hand in setting criteria for an abnormal Lead IV, he makes no corresponding requirement, such as a deviation of the RS-T segment. He regards Lead IV abnormal whenever the T-wave is "absent" or "upright" but does not stress an equally significant shallow or inverted T-wave in Lead I. In conformity with previous articles, here too, the writer presents a case to illustrate that an abnormal Lead IV may persist for a long time after a coronary occlusion. He does not mention, however, that the accompanying standard leads also show a definitely abnormal T-wave in Lead I, which is equally important.

These articles and case reports, dealing with chest leads, are interesting and instructive in that they disclose a strong tendency to overemphasize the value of a diagnostic procedure which as yet has been but imperfectly mastered. This tendency bespeaks a wish, it seems, for an open sesame into the hidden realms and manifold sequestered channels that lead to a diagnosis in cases of myocardial disease. Practically all tracings presented as groups showing normal standard leads with abnormal chest leads, actually show abnormal standard leads as well. These abnormalities, to be sure, are not conspicuous. They are characterized by a shallow or inverted T-wave only; but the abnormalities in the standard tracings of the group are generally confined to Lead I or Leads I and II. Such findings are clearly abnormal and are often indicative of myocardial damage. This was recognized very early in electrocardiography. Even Einthoven[9] in his early studies on the electrocardiogram clearly pointed out not only that T_1 and T_2 are normally always upright but that "if one finds a shallow or negative T-wave in Lead I or in Leads I and II, one deals with a diseased heart muscle, whose pathological deviation denotes a muscular insufficiency or *myodegeneratio cordis.*"

Furthermore, in cases cited in the literature as showing "conspicuous," "specific," or "pathognomonic" changes in Lead IV, while the accompanying standard leads presumably showed no abnormality, we find that such changes in Lead IV were indicated in the majority of cases only by an abnormally directed T_4. This, however, may not be taken as a pathognomonic change. It does not necessarily denote any more than an abnormally directed T_1.

A perusal of the records and a study of the data published in the literature, added to personal observations, point convincingly to the fact that a considerable number of electrocardiograms showing abnormal standard leads *are not* accompanied by abnormalities in Lead IV, and, furthermore, that an abnormal Lead IV with a normal standard electrocardiogram is extremely rare. The point seems to have been missed uniformly, that a conspicuous, abnormally directed T_4 cannot be present in an electrocardiogram which has a well-defined, normal, upright T_1. The two are incompatible.

The confusion that attended the early literature on chest leads (Lead IV) has been considerably clarified by the appearance of an article by Wood and Wolferth[10] on experimental coronary occlusion. This communication deals with carefully controlled experiments in which these workers occluded major branches of the coronary arteries through slits in the pericardium. With this technic, the anterior surface of the heart not being exposed, they were able to record electrocardiographic changes in chest leads of anterior as well as posterior lesions. The changes in the chest lead tracing, which they emphasize, is the RS-T deviation and not the much-misunderstood T-wave. The abnormal T-wave is a later change. The chest lead tracings in these modified experiments, they observed, resembled very closely those derived by leads taken directly from the hearts of their experimental animals. It was this observation which led to the use of the anteroposterior chest lead in human subjects suspected of coronary occlusion. Unfortunately, this publication appeared late. It was held up "in press" for about thirteen months. The cardinal points brought out by these experiments may be summarized as follows:

1. Occlusion of a major branch of a coronary artery produces an RS-T deviation within about two minutes.

2. With the R electrode placed anteriorly and the L electrode posteriorly, an *anterior infarct* produces a *depression* of the RS-T segment while a *posterior infarct* produces an *elevation*.

3. The results are similar to those obtained by leading directly from the heart.

These workers do not claim that their findings in the dog are necessarily transferable to man. In this article, as a further aid in diagnosis, they advise *also* additional chest leads, namely, from apex to foot and from dorsum to foot, Leads V and VI.

The subject of chest leads in the study of coronary occlusion takes on new and added interest as we follow the work of Wood and Wolferth and their collaborators. In one of their more recent publications[11] they present electrocardiographic observations and report necropsy findings in cases that were studied by means of three standard leads and three chest leads. They confirm their previous conclusion to the effect that in an acute anterior infarction, in addition to whatever the standard leads may show, chest leads, especially Leads IV and V, show a conspicuous negative deviation of the RS-T segment. They report, furthermore, that in this type of myocardial damage the initial negative component of the QRS, seen in the normal chest lead, tends to disappear. This has been pointed out also by Wilson, Barker, Macleod, and Klostermyer.[12] As recovery takes place, Wood and Wolferth maintain that the negative RS-T deviation gradually gives way to an upwardly directed T-wave; but that the initial negative component of the QRS which disappeared during the acute injury does not tend to reappear for some time.

To this observation the writers attach considerable importance. They believe that an absence of the characteristic initial downstroke of the ventricular complex in chest lead tracings denotes a residual stigma. In other words, that the absence of a Q-wave in Leads IV and V may be taken as presumptive evidence of a prior injury to the anterior ventricular wall along the course of the anterior descending branch of the left coronary artery. This is an interesting observation indeed and, if confirmed in a sufficiently large series of cases, will serve to establish the value of chest leads more securely as a routine procedure in clinical electrocardiography.

In this article the writers reiterate their previous statement to the effect that in coronary artery occlusions which produce infarctions of the posterior ventricular wall, chest leads "often show no abnormal findings." In such lesions it is well known that changes in the standard Leads II and III stand out preeminently and by far overshadow the chest leads. Yet, since in these lesions standard Leads II and III as well as chest Leads IV and V generally show also conspicuous negative deflections of the first limbs of the QRS complexes, namely conspicuous Q-waves, the chest lead tracings may serve an important purpose in possibly disclosing a previous anterior wall injury. This they might disclose by the absence of Q-waves, the residual stigma discussed in the foregoing paragraph.

In the light of the foregoing, chest leads may then be viewed as being of aid at least in two perplexing clinical problems relating to injuries of the left ventricular myocardium. A conspicuous deviation of the RS-T segment may be regarded as being indicative of an acute or recent injury, and the "residual stigma"—absent Q-wave—of an old injury to the wall of the left ventricle.

Thus the literature on chest leads, although in the main insufficiently informative, leads us nevertheless to the conclusion—essentially on the basis of the work of Wolferth and Wood—that evidences of certain types of myocardial damage may be disclosed by special leads in which one electrode is located over the precordium. This does not imply that the methods employed at present necessarily serve fully to carry out this purpose. In fact, there remains a seeming need for a proper appraisal of the methods now in use, particularly since chest leads, judged by the popularity they have attained, probably are destined to remain as an integral part of clinical electrocardiography.

In order to maintain a proper perspective in our endeavor to evaluate special leads as aids in clinical electrocardiography, let it be recalled that electrocardiography by means of chest leads is not new. In fact, it is one of the oldest of cardiographic procedures. The first human electrocardiogram ever reported was derived by means of a chest lead. Waller,[13] using the capillary electrometer in the study of the electrical effects of the human heart and desiring tracings with maximal deflections,

employed apex leads. Einthoven and deLint,[14] in a study of the relative forms and amplitudes of the principal components of the electrocardiogram in human subjects under alternating conditions of rest and vigorous exercise, found it convenient to use chest leads. It was their object to record the greatest possible deflections in order that they might evaluate minor differences in the amplitudes of corresponding complexes, as a result of removal of vagus tone by exercise.

Shortly after the introduction of the string galvanometer, however, chest leads were discarded as a routine procedure in the study of the electrical effects of the human heart. The string galvanometer yielded ample deflections in limb leads. Furthermore, the limb leads finally chosen by Einthoven had proved to have certain remarkable properties not possessed by chest leads. They were found to be related to one another and to a common hypothetical resultant electrical axis, so that all three could be expressed as functions of a single variable. This interrelation permitted interesting calculations as to the value of the manifest body potential as well as to the behavior of the electrical axis in hearts of certain size and configuration.[15] In addition, the constancy in form and amplitude of any one of the three limb leads in relation to synchronous events in either of the other two leads stood out in great contrast to the inconstancy of tracings derived by means of chest leads. Soon after the introduction of the string galvanometer, therefore, particularly as a result of the recognition of the properties of limb leads, it was a natural consequence that chest leads as a routine should be discarded. After this, chest leads may be said to have been employed only in special investigations, especially in those concerned with the study of individual components of the electrocardiogram in certain types of abnormal heart action, or in the study of special physiological problems dealing with the spread of the excitation wave and the distribution of the cardiac potential. Some of these special investigations by means of chest leads are particularly noteworthy in that they have dealt with fundamental problems in electrocardiography.

Lewis,[16] in demonstrating that the oscillations in the electrical curves of auricular fibrillation emanate from the auricles, employed combinations of precordial electrodes. He had shown that these oscillations became more and more conspicuous as the exploring precordial electrode approached the vicinity of the right auricle.

Wilson,[17] in a study of the potential differences produced by the heartbeat within the body and at its surface, employed precordial electrodes. It was in this study that he made the interesting observation that in the case of chest leads "it is the electrode near the heart which determines the form of the ventricular electrocardiogram." He showed also that "it matters little where the second electrode is placed, providing it is sufficiently far away from the heart."

In a study of the relation between the anatomical and electrical axis of normal as well as hypertrophied hearts, Cohn and Raisbeck[18] used symmetrically arranged chest electrodes, the locations of which on the anterior chest wall corresponded to the apices of a rotating equilateral triangle.

With the aid of precordial electrodes, Wilson and his coworkers have made several valuable observations on the nature of bundle-branch block. By means of serial precordial leads from several points across the lower anterior chest, from right to left, they were able to show the order of excitation of the ventricles in human bundle-branch block.[19] More recently[20, 21] with a similar system of exploring chest electrodes but with the additional aid of an ingenious device affording a second, strictly neutral electrode, they have been able to decipher certain types of abnormal human electrocardiograms as belonging to the category of right bundle-branch conduction defects. This method of study (unipolar electrocardiography) has tremendous and far-reaching possibilities. It may prove to be the key to an entirely new approach in the study of electrocardiography.

A report of Wilson, Barker, Macleod, and Klostermyer[12] is of particular interest in connection with the subject of this paper. This communication may be deemed a connecting link between the many and diverse electrocardiographic studies by means of special leads in the past and the more recent work of Wolferth and Wood which has since led to the present popularity of chest leads as a routine cardiographic procedure. This report is primarily concerned with anomalies in the initial ventricular complex (QRS) in coronary occlusion as deciphered by the standard leads. In this report the writers, however, recorded tracings by means of chest leads as well, and they point out also characteristic changes in the initial as well as the terminal ventricular complexes of chest lead tracings in cases of anterior and posterior cardiac infarction as a result of coronary thrombosis.

The subject of chest leads naturally leads one to the experimental, pathological, and clinical observations of Wolferth and Wood,[1, 2, 10, 11] which in the aggregate mark an important milestone in electrocardiography. Their observation of an early, conspicuous RS-T deviation in direct leads employed in experimental coronary occlusion and, particularly, their further observation that such deviations in the terminal ventricular complex when recorded by means of an anteroposterior chest lead are essentially the same as those derived by direct leads, has naturally suggested the use of chest leads in human subjects suspected of coronary occlusion. Throughout their publications they lead toward one seemingly cardinal point: namely, that in certain cases of acute coronary occlusion, especially those producing infarction in the course of the anterior descending branch of the left coronary artery, the chest lead may show the earliest evidence of an acute myocardial damage. Such a

lesion is indicated by a deviation of the RS-T segment, which, as recovery takes place, is followed by an abnormal direction of the T-wave. In the case of their special chest lead, designated as Lead IV, the abnormal T-wave is positive—directed upward. This chest lead of Wolferth and Wood, together with Leads V and VI which they subsequently suggested, constitutes the conventional set of chest leads now generally employed in clinical electrocardiography. As such they merit special comment. This is particularly true of Lead IV.

Lead IV, then, is a special lead in which two electrodes are placed in contact with the chest wall; one, the right arm electrode, in the vicinity of the cardiac apex, and the other, the left arm electrode, in the left paravertebral space above the level of the angle of the scapula. The tracing derived by this lead is well known. Its features have been care-

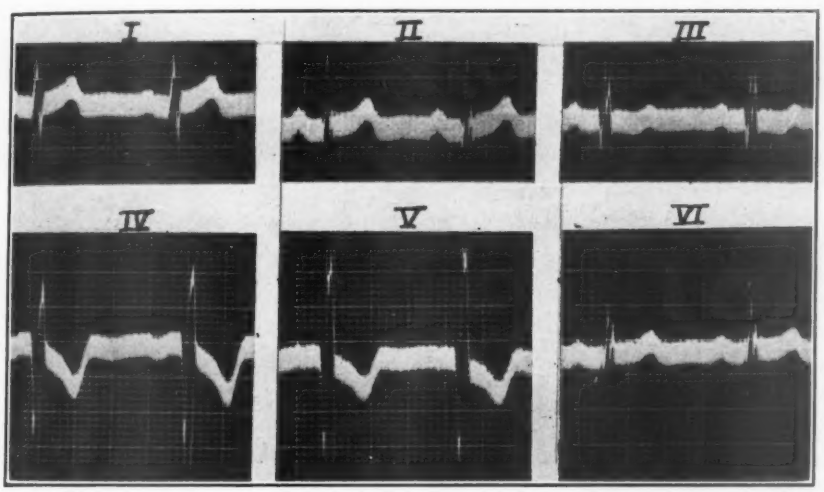

Fig. 1.—Standard Leads I, II, and III compared with the conventional chest Leads IV, V, and VI. For description see pages 811 and 812.

fully described at the time of its introduction and have been subsequently verified by others in studies aggregating hundreds of normal subjects.[5, 6, 7, 8, 22] The tracing is characterized by: (a) an inverted auricular (P) wave, (b) a diphasic initial ventricular complex (QRS), and (c) an inverted terminal ventricular (T) wave.

Besides these characteristics, the individual components of this electrocardiogram have other peculiarities. The auricular P-wave is very shallow; the initial ventricular complex is large and begins with a downstroke—a Q-wave; the T-wave is large. The RS-T segment has practically no isoelectric period (Fig. 1). Occasionally there is normally present in Lead IV a slight negative deviation of the RS-T segment, of one or two millimeters. This is probably an artefact due to overshooting of the galvanometer string.

These criteria are best remembered if we regard Lead IV as a magnified, partly inverted Lead I rotated through an angle of 90°, bringing the lead axis into a plane parallel to the sagittal instead of the coronal plane of the body. The magnification is confined to the ventricular complex and is due to the fact that one electrode is situated in a region where the heart is nearest to the chest wall. The inversion of the principal components of this tracing, as compared with those of standard Lead I, is due to the right arm electrode being situated in the vicinity of the cardiac apex. (In standard leads this electrode is nearer to the basal region of the heart.) Rotation is suggested by the shallow negative P-wave and the diphasic QRS.

As has been stated, Wolferth and Wood advocate a set of three chest leads. In addition to Lead IV they employ also Leads V and VI. The tracing of a normal Lead V is essentially of the same general configuration as that of Lead IV, in spite of the fact that the electrode which in Lead IV is located near the left scapula is attached in this lead to the left foot. The reasons for the similarity between these two tracings will be discussed in another paragraph. Lead VI, on the other hand, bears practically no resemblance to either of the other two. This is a lead from the left scapula to the left foot. It yields a rather indistinct and a considerably stunted tracing. It generally resembles a miniature Lead III (see again Fig. 1).

The carefully described criteria for Lead IV (or for any chest lead) are but gross at best. There are many factors to prevent a constancy in the form of chest lead tracings. Among these are: dislocation of the anatomical axis of the heart in extremes of habitus, as in short wide chests or long narrow chests; the amount and the kind of media interposed between the cardiac apex and the electrode, as in obesity, emphysema, or intrathoracic effusions; inaccuracy in locating the apex impulse; or shifting of the "apical" electrode. The last mentioned factor is of importance. Hoffman and Delong[7] in their study of normal lead IV found appreciable alterations in their tracings on slight changes in the position of the anterior electrode. Wood, Bellet, McMillan, and Wolferth[11] also stress this. They caution, in fact, that when "small electrodes are used, a relatively small change in the position of the anterior electrode may cause considerable alteration in the tracings." The effect of changing the position of the anterior electrode on the form of the ventricular electrocardiogram is illustrated in Fig. 2.

Since it exerts a definite controlling effect on the form of the resulting curve, the anterior electrode in chest leads may be designated as the principal electrode. The posterior electrode, on the other hand, may be termed an indifferent or at best a secondary electrode. That the position of this electrode is comparatively immaterial has been pointed out by Wilson[17]—to quote: ". . . the position of the second electrode so long as it is relatively distant from the heart has little effect on the ventricular

electrocardiogram." This is verified and illustrated in Fig. 3. Serial electrocardiograms were taken with a fixed anterior electrode and a shifting posterior electrode, placed successively on the right arm, right scapula, left scapula, left lumbar region, and left foot. They show no appreciable alteration in the form of the ventricular curve, except for

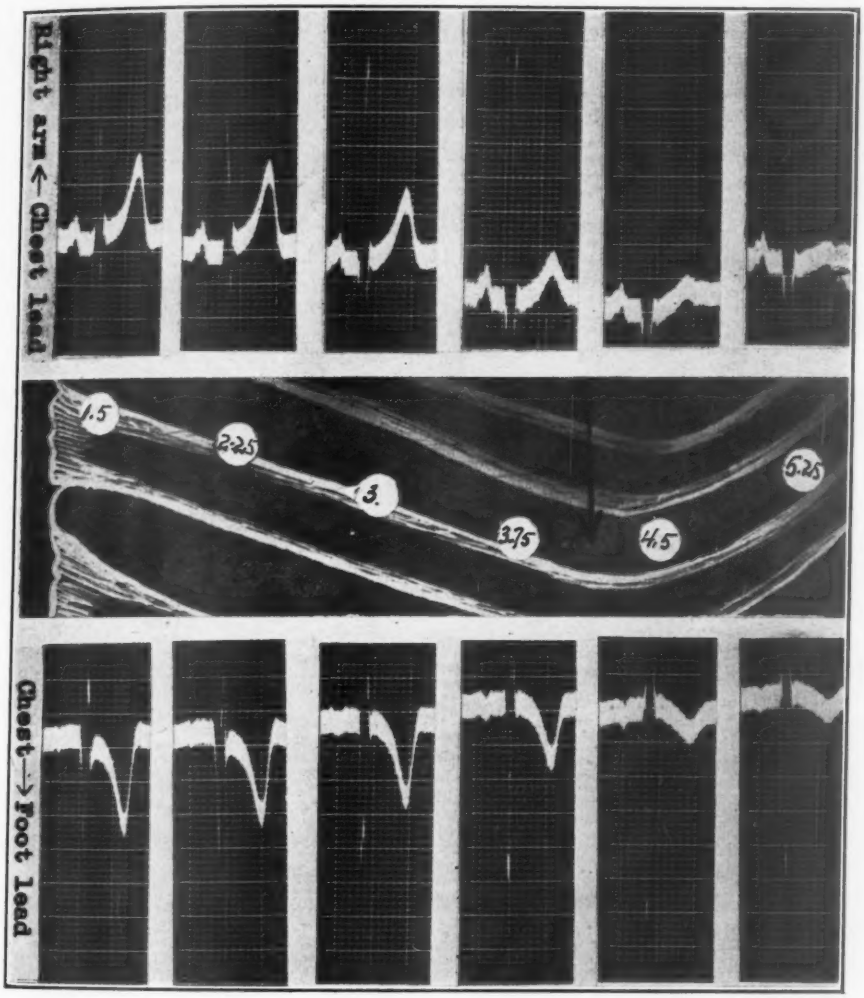

Fig. 2.—The effect of shifting the principal electrode on the form of the ventricular electrocardiogram.

As indicated in the diagram accompanying the graphs, the principal electrode was applied over successive zones approximately 0.75 of an inch apart, along a line beginning at a point 1.5 inches from the midsternal line and extending to the left for a distance of about 3.75 inches, or 5.25 inches from the midsternal line. The region of the apex impulse is indicated by an arrow.

In both the upper and lower rows the first four graphs, recorded from zones between the left sternal margin and cardiac apex, show T-waves of fairly constant form. The last two graphs, recorded from zones between the apex impulse and a point 1.25 inches beyond, show a sharp fall in the amplitude of the T-waves and a corresponding rise in the QRS complexes. The upper row of graphs were recorded by leads from right arm to chest, and the lower row, by leads from chest to foot. The chest electrode was attached to the left arm cable. Its diameter was approximately 1 inch. The chest foot lead is identical with Lead V of Wolferth and Wood.

slight changes in amplitude.* Even if tracings were not presented to demonstrate this, ample evidence may be had by comparing Leads IV and V of Wolferth and Wood. Lead IV, as has been stated, is derived by means of an apical electrode and a second electrode in the region of the left scapula, while Lead V is derived by means of the same apical electrode but with the second electrode attached to the left leg or foot. Yet, the forms of these two tracings are similar in many details, giving evidence of the "indifference" of the second electrode. So obvious is the similarity between these two tracings, although derived by two distinctly different leads, that some laboratories have adopted the use of Lead V instead of Lead IV as a matter of bedside convenience in clinical routine.

The manner of application of the chest electrodes (R electrode anteriorly and L electrode posteriorly), as originally adopted by Wolferth and Wood, is open to some objections. To those with limited experience, Leads IV and V may appear at first glance as somewhat distorted, magnified, mirror pictures of Lead I of the standard electrocardiogram. And there is some reason for this impression. Lead IV does "mirror" primarily the standard Lead I. Abnormalities in Lead IV, when accompanied by abnormalities in the standard leads, are generally paralleled by Lead I only. Both, Lead IV and Lead I generally depict the same lesions of the ventricular myocardium, namely, anterior surface lesions. Yet, when these two tracings are viewed side by side, one is struck by the marked dissimilarity between their synchronous components. Synchronous deflections in the two leads have diametrically opposite directions. This at first glance tends to some measure of confusion. The chest lead tracing has a strange configuration. In fact, it requires the study of a new set of criteria in which the principal components of the electrical curve are expressed in negative values.

Yet, there is some justification for the manner of application of electrodes as advocated by Wolferth and Wood. If the apical electrode is to represent the exploring electrode used in experimental direct leads and if it is desired that the potential variations beneath this electrode be recorded in positive values, the R electrode must be applied anteriorly. In fact this is precisely why an "inverted" Lead IV came into clinical use. As has been stated, Wolferth and Wood, employing direct leads in experimental work, used the R electrode as the exploring electrode. It was with this technic that they first recorded characteristic RS-T deviations in experimental coronary occlusion, showing a *depression* of the RS-T segment in *anterior lesions* and an *elevation* in *posterior* lesions. By a cleverly contrived experimental procedure, they showed furthermore that if the anterior surface of the heart was not exposed, they could duplicate these electrocardiographic changes by means of chest leads. To demonstrate the striking similarity between curves derived by direct

*This is not true for the auricular P-waves. See again Fig. 3.

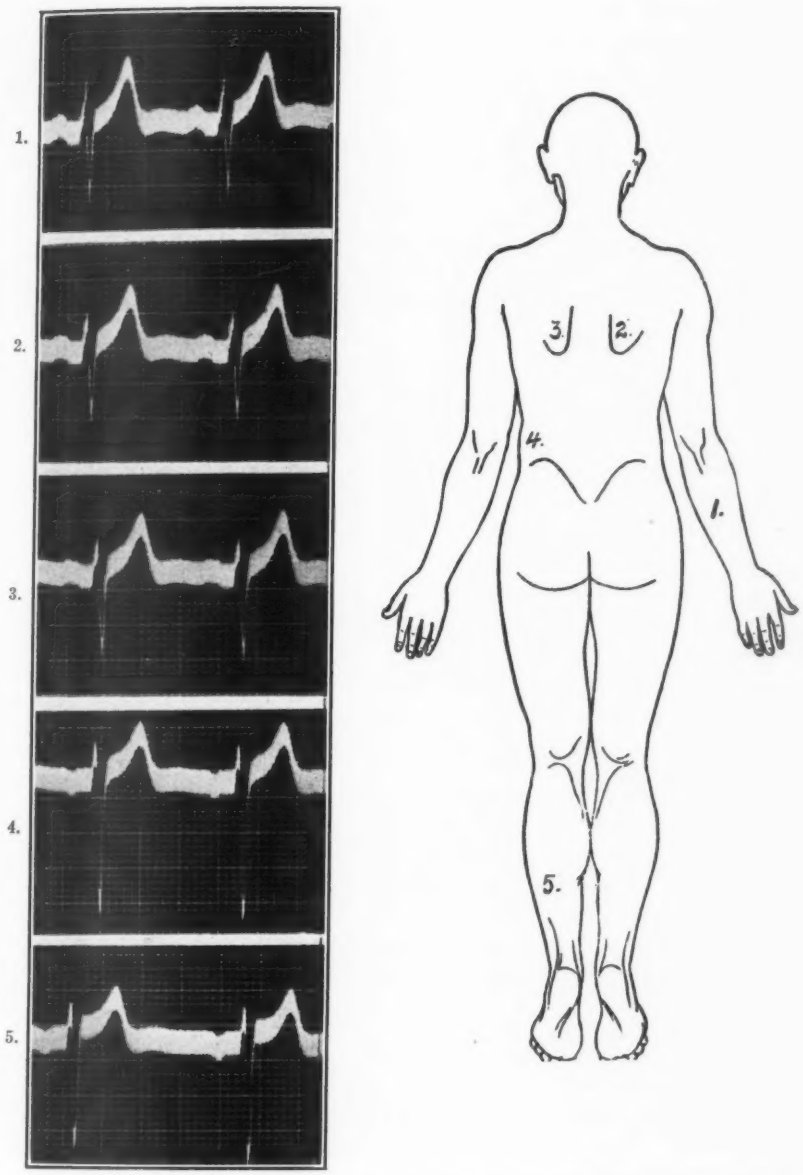

Fig. 3.—The effect of shifting the second or "indifferent" electrode on the form of the ventricular electrocardiogram.

As indicated by the numerical notations in the diagram accompanying the graphs, the right arm electrode was applied successively over widely separated regions on the surface of the body. The graphs show that the ventricular curve is practically unaffected except for slight changes in amplitude. On the other hand, the auricular P-waves are definitely altered.

In all these "leads" the principal electrode was held in exactly the same fixed position, in the region of the apex impulse. See footnote on page 826.

leads and those derived by chest leads, they naturally had to employ the same relative method of application of electrodes, that is, the R electrode as the anterior electrode. This had automatically set criteria for their chest lead analogous to those of their direct lead; and these criteria, expressed in negative ordinates, were eventually transferred, with the clinical adoption of chest leads, to the study of coronary occlusion in man.

Nevertheless, this manner of grouping of chest electrodes when carried over to clinical investigations has, it seems, certain disadvantages. Ever since its introduction, Lead IV has been advocated as an *aid* to the standard leads. It was never to replace but merely to complement the standard leads. The standard electrocardiogram and the chest lead tracing were intended to appear as a group. Such being the case it would seem desirable that some measure of symmetry characterize this group. To this effect a chest lead, taken with the L electrode applied anteriorly instead of the R electrode, would afford such a symmetry in that all deflections in the chest lead would then correspond in direction to those of the standard leads, for all identical events in the cardiac cycle. Lead IV as recorded at present fails to afford this much desired symmetry. In fact, in its present form it has necessitated the learning of a set of new criteria depicted in negative ordinates.

Furthermore, the scapular application of the posterior electrode as employed in the conventional Lead IV seems unnecessary. At times it may even prove somewhat burdensome. In the case of an acute coronary occlusion in which the chest lead is presumed to subserve the greatest usefulness, the patient may be and frequently is acutely ill; at times he is moribund. The application of a posterior electrode under such circumstances may offer a difficulty to the operator and an annoyance to the patient. In such a case simplicity of technic is most desirable. This is probably the reason why some clinicians have adopted the use of Lead V alone and have discarded the original Lead IV.

The numerical designation of chest leads introduced by Wolferth and Wood is also open to objections. The designation "Lead IV" implies a relationship to the standard Leads I, II, and III. Actually, while the standard Leads I, II, and III are strictly related to one another (components of a common vector), Lead IV bears no such relationship to any one of them whatever. As a matter of fact, Lead IV is not even a fixed lead. The principal electrode which actually determines its form is at times applied by some workers to the left parasternal line in the fourth space, and at other times to the region of the cardiac apex. The numerical designation of Lead IV does not specify the point of application of the principal electrode, which, as has been shown, actually determines the form of the resulting electrocardiogram. The only thing about this lead that may be regarded as relatively fixed is the posterior electrode; and this, as has been stated, is practically immaterial. In the case of

standard leads the numerical designation of a lead implies a specific location of the electrodes,* and the numerical designation employed carries the same connotation wherever electrocardiography is done. This, not being true for chest leads, suggests the necessity of more specific designations. This statement takes on added weight if we take into consideration the fact that the present popularity of chest leads has prompted many investigators to "tap" the chest in innumerable directions for special chest leads. To designate all such leads by numbers will ultimately necessitate the use of a comprehensive code book.

Chest leads, it seems, should be designated by convenient abbreviations of well-known anatomical landmarks which would indicate the approximate location of the principal electrode. This would lead to a clearer visualization of the technic employed by different workers and would enable one to follow the progress of the work initiated by Wolferth and Wood with greater facility. Such a regional anatomical designation would lead, furthermore, to a uniformity of nomenclature expressed in a familiar terminology.

The common sites of location of the principal electrode selected for chest leads at present are: the region of the apex impulse, normally in the fifth space and midclavicular line; the left pectoral region, in the fourth left interspace, about two inches to the left of the midsternal line; and, rarely, the right pectoral region, in the fourth right interspace, about two inches to the right of the midsternal line. These regions may be conveniently designated as the apical, left pectoral, and right pectoral regions, respectively. If the location of the second electrode is chosen and held as a fixed point and if the principal electrode is placed arbitrarily over any one of the regions mentioned above, the resulting lead may then be designated according to the region at which the principal electrode is attached; namely, as an apex lead, a left pectoral lead, or a right pectoral lead; or by the abbreviations, Ap, Lp, and Rp leads, respectively. Such a designation of a chest lead is desirable in that it indicates the location of the principal electrode.

The location of the second electrode, although relatively immaterial, may nevertheless be chosen also with definite purposes in view. We have noted, for instance, that in the conventional chest leads, Leads IV and V of Wolferth and Wood, the auricular complex, P, is generally very shallow and inverted and that at times it is completely absent. We have noted also that, while the location of the second electrode has little influence on the ventricular electrocardiogram, it does influence its amplitude in some degree. The location of the second electrode may therefore be chosen with a view of deriving a tracing which will yield the largest possible deflections in the components of the ventricular portion of the electrocardiogram and which at the same time will include a well-defined auricular P-wave.

*Specific in the sense expressed in footnote on page 801.

The site of application of the second electrode which affords these two features in a chest lead is found to be a most convenient one. It is the right arm or right shoulder. It is a curious and historically interesting fact that as early as 1900 Einthoven and deLint,[14] in search for a lead that would yield the largest possible deflections in their electrocardiogram, came to the conclusion that this requirement was fulfilled best by the right arm apex lead. To quote them verbatim: "Wir legten die Elektroden on diejenigen Stellen des Körpers an, welche die grössten Schwankungen des Potentialunterschiedes zeigten . . . auf der eine Seite der Brustwand nahe by dem Apex Cordis, auf der anderen Seite die rechte Schulter order der rechte Arm."

By the use of a right arm chest lead, then, we can record a tracing which depicts well-defined auricular as well as ventricular complexes and which, at the same time, yields maximal deflections with the galvanometer string at standard sensitivity. These are clearly desirable features in a chest lead. Futhermore, since in a right arm chest lead the right arm electrode is the fixed secondary electrode and the left arm electrode is the one which is employed as the principal electrode, we derive a tracing by this lead which has the added feature of symmetry with the standard leads in that its main deflections correspond in direction with those of the standard leads. This is in keeping with the original intention of Einthoven, who so arranged his circuit for patient and galvanometer that normally all major deflections of his electrical tracings were expressed in positive ordinates. The right arm chest lead has still another and a much desired advantage in that it requires but a single chest electrode. This is a readily recognized convenience in clinical electrocardiography at the bedside.

In summary, then, the right arm chest lead is serviceable as a routine chest lead for clinical use because it embodies the following:

(a) A tracing derived by this lead represents all components of the cardiac cycle, auricular as well as ventricular, in a well-defined form.

(b) All principal deflections in the tracing are maximal for a galvanometer of standard sensitivity.

(c) All principal deflections in the tracing conform in direction with synchronous deflections in the standard leads, thus lending symmetry to the group.

(d) The chest lead is convenient for bedside use in that it requires but a single chest electrode.

Figure 4 shows a group of electrocardiograms taken from a young woman in good health, to illustrate the relative form of the right arm apex (R-Ap) lead as compared with standard leads and several special leads.

It might seem that the introduction of a special lead, the right arm chest lead, would meet with objections on the ground that since the conventional leads have been in use for almost three years, their criteria

being familiar, a change at this time would be inconvenient. But this special lead, if employed, need not necessarily replace all conventional chest leads now in use. In fact, as will be shown, the writer has found it convenient to employ one of the leads of Wolferth and Wood (their Lead V) as a companion chest lead without any change in the arrangement of electrodes. An objection might also be raised on the ground

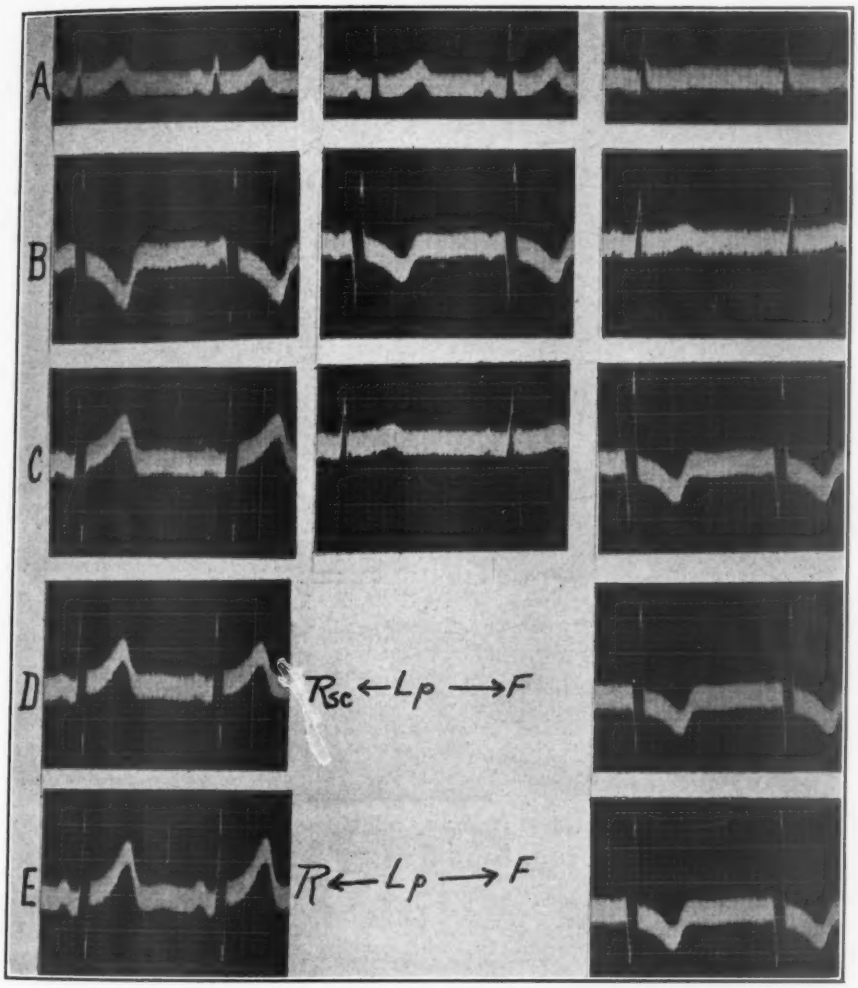

Fig. 4.—Tracings derived by the right arm chest lead and its companion lead, the chest foot lead, as compared with those derived by standard leads and several special chest leads.

In each case the chest electrode was located over the fourth interspace about 2 inches to the left of the midsternal line.

A. Standard Leads I, II, and III.
B. Chest Leads IV, V, and VI.
C. Posteroanterior chest lead; reverse of B.
D. Right scapula, chest and chest foot leads.
E. Right arm chest and chest foot leads.

The *right arm chest* lead tracing shows well-defined auricular and ventricular complexes, the components of which correspond in direction with synchronous deflections in the standard leads.

that since Leads IV and V have been recently shown to disclose evidences of residual injury to the anterior surface of the left ventricle (absent Q-wave), this information might be lost by the adoption of the right arm chest lead. Actually, whenever Leads IV and V show absence of Q-waves, the right arm chest lead depicts its equivalent by showing an absence of the R-wave; that is, the ventricular electrocardiogram of the right arm chest lead begins with a conspicuous initial downstroke. This

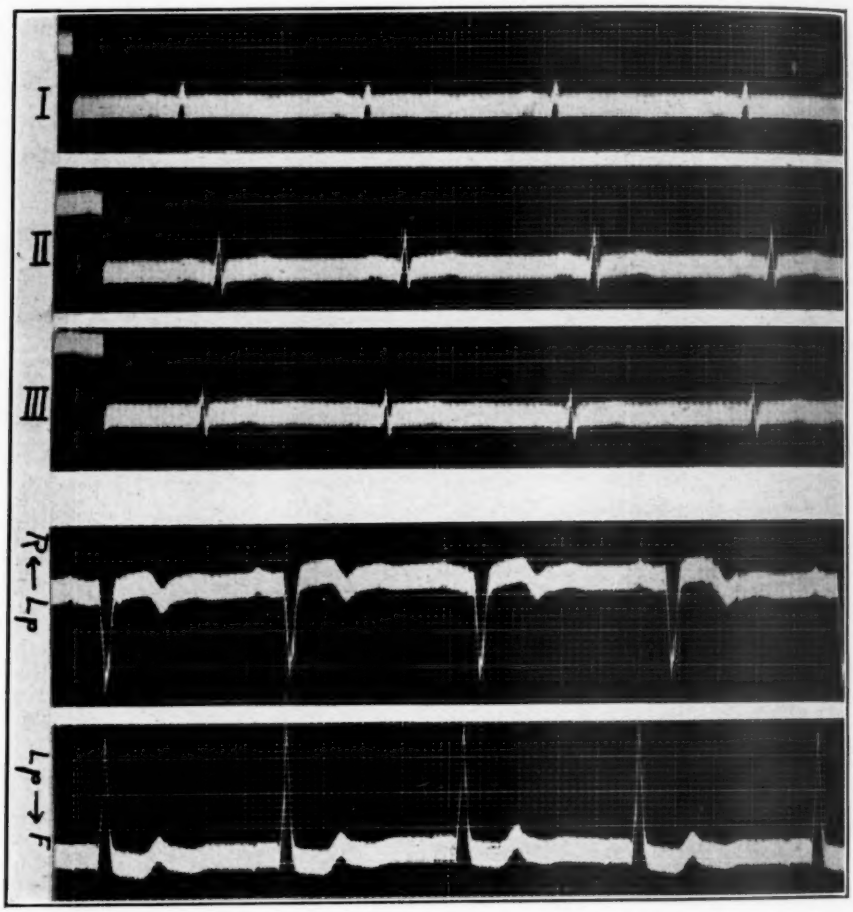

Fig. 5.—Tracings derived by standard leads, the right arm chest lead, and the chest foot lead in a case clinically suggestive of an old injury to the anterior wall of the left ventricle.

The chest foot lead (Lp→F), in conformity with the observations of Wood, Bellet, McMillan, and Wolferth,[11] shows "absence of the Q-wave." The tracing of the right arm chest lead (R←Lp), on the other hand, shows its counterpart, namely, an absent R-wave.

is in conformity with changes often seen in standard Lead I in such cases. It serves as a conspicuous analogue of the Q_1 type standard electrocardiogram, which has now been accepted as an index of previous injury to the anterior portion of the left ventricle. Fig. 5 shows tracings derived

by standard leads, the right arm chest lead, and the chest foot lead (Lead V) in a patient presumed to have an old myocardial injury along the path of the anterior descending branch of the left coronary artery.

The right arm chest lead, therefore, records all the cardinal changes in the ventricular complex which we have learned to regard in conventional chest lead tracings as being indicative of myocardial damage; namely, abnormally directed T-waves and abnormalities in the direction of the initial deflection of the QRS complex. In fact, since these are

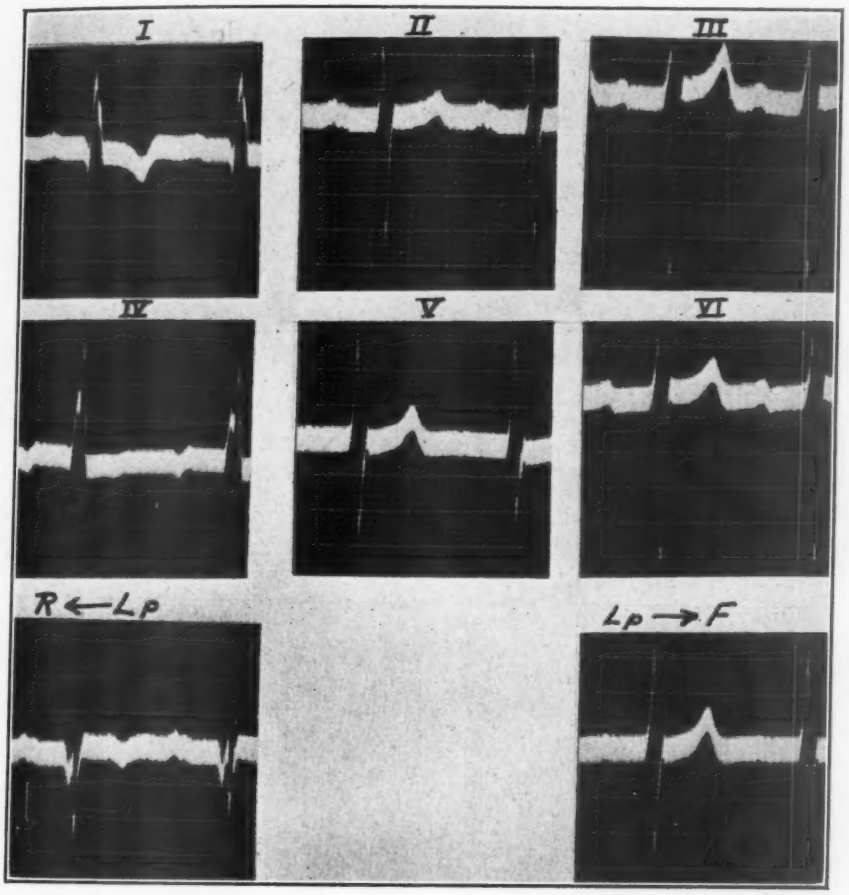

Fig. 6.—Tracings in a case in which Leads IV and V differ markedly in general outline although they both show the same major abnormalities, namely, abnormal T-waves and absent Q-waves.

Right arm chest lead tracings show the equivalent abnormalities, namely, abnormal T-waves and absent R-waves. The R ← Lp lead tracing possesses all characteristics of Lead IV, and the Lp → F lead is identical with Lead V.

the only changes in chest leads which may be deemed of diagnostic value at present, it seems that the right arm chest lead would suffice as a routine chest lead in all cases in which myocardial damage is suspected. It yields all information generally regarded as of diagnostic value in these cases.

It is not claimed, however, that the right arm chest lead is a substitute for all chest leads. The study of chest leads in clinical electrocardiography is of comparatively recent date and may not be restricted. It has been found that certain chest leads which normally resemble each other closely may, nevertheless, differ widely in minor details when derived from persons having chronic fibrotic myocardial lesions. Leads IV and V, for instance, while generally alike in normal hearts and while generally recording the same gross deviations in well-defined myocardial involvement as a result of coronary occlusion, may occasionally differ in details the meaning of which, up to date, is entirely foreign to us. Fig. 6 is an example of such a case. It seems desirable, therefore, for purposes of further study (not necessarily for routine clinical use) that a companion chest foot lead be taken with the right arm chest lead. In the light of our present knowledge this may afford no additional information. However, since we do occasionally encounter cases in which the two chest leads differ in certain details—although, in the main, equally informative with respect to findings which have become familiar—it is desirable that such records be taken and filed for future studies.

The technic of taking the right arm chest lead together with Lead V at the bedside is carried out as follows: The three standard leads are taken. Then the cable of the left arm electrode is detached and is connected to the chest electrode* applied to the region of the cardiac apex (or any other pectoral area). In this position the operator selects on the control board of his instrument, Leads "I" and "III" successively. The first of these (Lead "I") is naturally the right arm chest lead here advocated, and the other (Lead "III") is the companion chest foot lead, which is precisely Lead V of Wolferth and Wood.

Since it is the principal electrode (the one nearest to the heart) which determines the form of the resulting curve, the use of the right arm chest lead was extended in an endeavor to explore different pectoral zones. The principal electrode was applied successively to the right pectoral, left pectoral, and apical regions, the second electrode having been fixed in each case at the right arm. The leads were designated as the right pectoral (Rp), left pectoral (Lp), and apical (Ap) leads, respectively. Each of these leads seems to serve as a distinct source of information. In the right pectoral (Rp) lead the auricular P-wave is conspicuous, especially in cases in which there is clinical evidence of enlargement of the right auricle. In the left pectoral (Lp) lead the terminal ventricular complex, T, stands out most prominently. The apical (Ap) lead, on the other hand, accentuates the initial ventricular complex.

The right pectoral (Rp) lead may be employed to record tracings of auricular activity in cases of auricular fibrillation or other conditions

*There is a wide choice of chest electrodes. Those employed in the cases illustrated in this article were of the self-retaining type, built on the principle of vacuum cups to assure against possible shifting of the principal electrode. The size of the electrode never exceeded 1.5 inches in diameter.

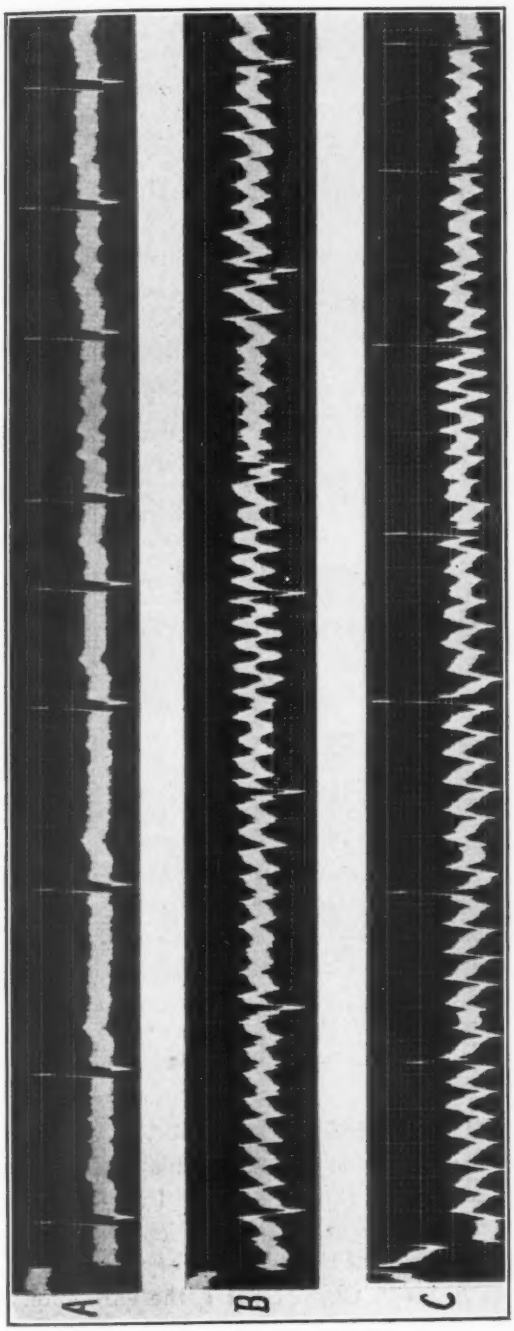

Fig. 7.—A case of auricular fibrillation recorded by *A*, standard lead II; *B*, the right arm right pectoral lead; and *C*, the right pectoral foot lead.

The variations in the form, rate, and rhythm of the auricular waves are brought out conspicuously by both the right arm right pectoral and the right pectoral foot ($R \leftarrow Rp \rightarrow F$) leads.

in which the right auricle is enlarged. Such a tracing is presented in Fig. 7. In this tracing the auricular waves are remarkably clear, and one can count them accurately over long periods. It also serves to emphasize the profound variations that take place both in rate and contour, in the auricular waves in fibrillation. Another tracing recorded by the right pectoral (Rp) lead is presented in Fig. 8. This tracing shows clearly deciphered auricular P-waves within the different portions of the ventricular complexes, not quite as sharply outlined in the standard tracings.

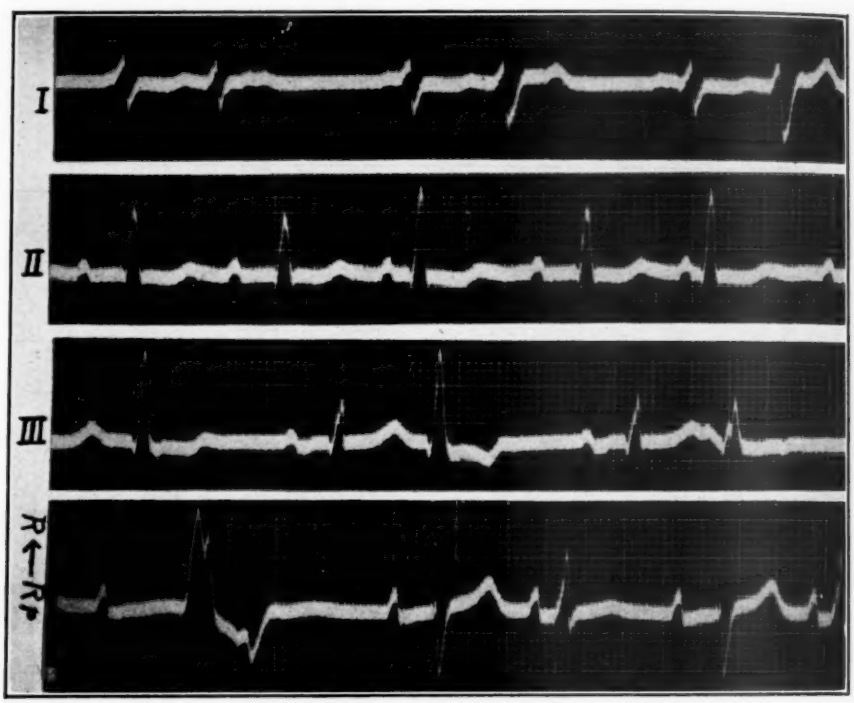

Fig. 8.—Tracings derived by standard leads and the right arm right pectoral (R ← Rp) lead in a case presenting clinical evidences of an old mitral valvular defect with heart failure. The auricular P-waves are largest in the chest lead tracing, and they are clearly defined even when superimposed on an ectopic ventricular complex.

In the left pectoral (Lp) lead the terminal portion of the ventricular complex is deciphered most conspicuously. This lead therefore seems most serviceable in cases in which standard Lead I is of very low voltage. Clinical cases suggestive of myocardial infarction along the course of the anterior descending branch of the left coronary artery at times yield standard electrocardiograms in which Lead I, the most important lead, although abnormal, may nevertheless be regarded by some as "inconclusive" because of a low amplitude of the T-wave. In such cases the left pectoral (Lp) lead will generally serve to accentuate the terminal

ventricular complex (RS-T and T) with all its abnormal deviations sufficiently to render the tracing acceptable as evidence of the myocardial damage presumed to have taken place. Fig. 9 is a striking example of such a case. The electrocardiograms presented in this figure were recorded shortly after the clinical "coronary episode"—a few hours after. Experience has taught us to regard the shallow standard Lead I in such a case as being abnormal and definitely pointing to the diagnosis of a focal myocardial involvement. Yet, since some may regard it as "inconclusive," the Lp chest lead should accompany the standard electrocardiogram in order to accentuate the RS-T deviation sufficiently to remove all doubt.

The apex (Ap) lead is essentially for the same purpose as the left pectoral (Lp) lead, except that in the former the QRS is somewhat taller and the T-waves not quite as tall as in the latter. The apical

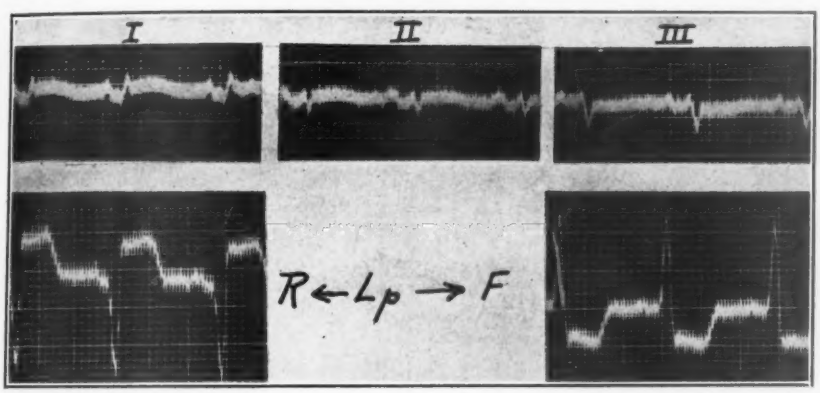

Fig. 9.—Tracings in a case of an acute left coronary occlusion, recorded by standard leads and by the right arm left pectoral and left pectoral foot (R ← Lp → F) leads, taken about six hours after the onset of angina pectoris.
The standard lead tracings are of very low voltage but Leads I and II show a characteristic high take-off of the RS-T segment. The chest leads magnify this deviation sufficiently to remove any doubt that might be occasioned by the low voltage in the standard leads.

application of the principal electrode has been the most common practice in chest leads. Yet for many reasons apex leads are least reliable. In employing this lead, there is usually some element of uncertainty as to whether the operator has really found the point of application of the principal electrode he has sought. The apex impulse, at best, is very elusive. This is particularly true in patients at an age when they are most liable to sustain a coronary occlusion. The chests of persons at middle age are often of the obese and hypersthenic type; their lungs, emphysematous; and their hearts, especially after an acute injury, may be too feeble to produce a palpable impulse. It is likely also that in his desire to locate the apex impulse accurately the operator at times applies the electrode beyond the boundary of the heart. This probably accounts for some of the cases which show marked differences in the chest leads

on slight shifting of the "apical" electrode.* Shifting of the electrode in an area well within the bounds of the apex impulse does not produce the same degree of difference in chest lead tracings (see again Fig. 2). In such cases, however, one is really recording tracings by, or what amounts to, the left pectoral (Lp) lead. In this lead the principal elec-

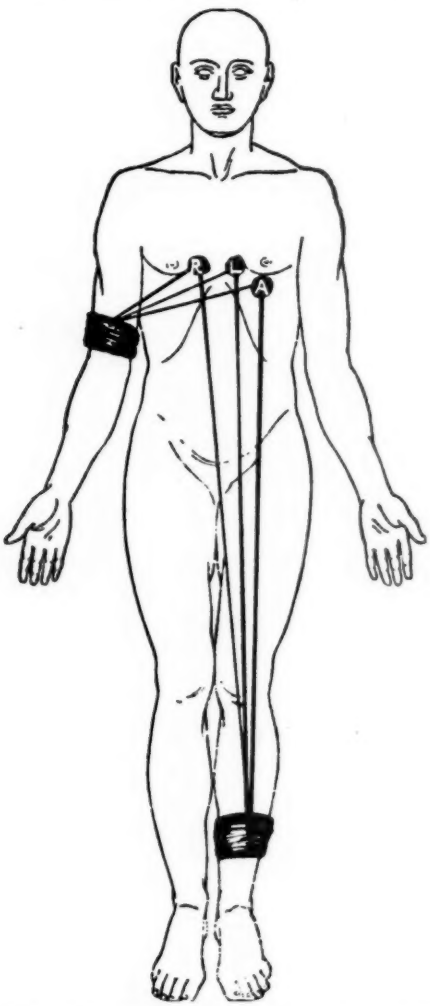

Fig. 10.—Arrangement of electrodes for the several right arm chest leads and their companion tracings. *R*, the (R ← Rp → F) lead; *L*, the (R ← Lp → F) lead; and *A*, the (R ← Ap → F) lead.

As the diagram indicates, a single chest electrode serves for all these leads, and the second or "indifferent" electrodes occupy the same positions as in the standard leads.

*The evaluation of the relative amplitudes of the QRS complexes in chest lead tracings is difficult at best. The apex, being the most mobile portion of the heart, shifts readily from beneath the electrode with each respiratory excursion of the diaphragm. An apical lead, therefore, often yields tracings which show marked respiratory variation in the amplitude of the initial ventricular complex. Furthermore, because of the large swing of the galvanometer string, standardization in chest leads is at times difficult and often inaccurate.

trode is situated approximately midway between the cardiac apex and the midsternal line.

It seems from the foregoing that, if only a single chest lead is intended to complement the standard leads, the object of the operator being merely to clarify such abnormalities in the electrocardiogram as may appear principally in Lead I (suggestive of anterior surface lesions), the left pectoral (Lp) lead is the chest lead of choice. As has been stated, this lead may be supplemented by its companion tracing, the left pectoral foot, Lead V of the conventional set of chest leads.

However, a single chest lead or, for that matter, a pair of companion chest leads (from the same point on the anterior chest wall), while helpful as an aid to the standard leads, is essentially limited in scope. The information it may yield is limited because a chest lead tracing is an expression of the electrical changes of those structures mainly which are nearest to the principal electrode. This is a singular property of chest leads and, as such, may be utilized to gain wider information. It enables one, even by way of gross plotting, to record electrical changes that emanate from certain structures in excess to those of neighboring structures. This can be accomplished by applying the principal electrode over selected zones beneath which a given structure, whose effects are sought, is presumably situated. Unfortunately, the posterior cardiac surface is not readily accessible for investigation by means of chest leads because it rests on the diaphragm. However, the anterior chest wall affords a ready approach to the study of structures that make up the anterior cardiac surface, namely, the right auricle and the two ventricles.

For a study of the electrical effects of the cardiac chambers that comprise the anterior surface of the heart, the right pectoral, left pectoral, and apical chest leads lend themselves conveniently. It seems desirable, therefore, that these chest leads be employed in electrocardiography either singly or paired with their companion leads, in addition to the standard leads, whenever a more general study of the electrical effects of the heart is intended. The procedure is not particularly time consuming. A diagram in Fig. 10 shows the arrangement of the electrodes for these leads. As has been suggested, they may be designated by convenient abbreviations of anatomical landmarks indicating the position of the electrodes. If employed as single leads, they may be recorded as:

$$\begin{aligned} R &\longleftarrow Rp \\ R &\longleftarrow Lp \\ R &\longleftarrow Ap \end{aligned}$$

or when employed in pairs, as:

$$\begin{aligned} R &\longleftarrow Rp \longrightarrow F \\ R &\longleftarrow Lp \longrightarrow F \\ R &\longleftarrow Ap \longrightarrow F \end{aligned}$$

These tabulations show at a glance that the secondary electrodes attached at the right arm and the left foot are fixed and occupy the same positions as in the standard leads; they show also that the principal electrode attached to the left arm cable has an arbitrary location over the anterior chest wall. The arrows indicate the directions of the major components of the electrocardiogram recorded by each lead.

In conclusion it might be added that no matter what form routine chest leads might eventually take, chest leads have apparently found a permanent place in clinical electrocardiography. However, since our present knowledge as to the meaning of chest lead tracings is still limited, it seems incumbent upon us not only to be cautious in our observations but also to be critical in evaluating observations recorded by others. Standard lead tracings are still to be regarded as the more reliable guides in clinical electrocardiography. The early warning of Wolferth and Wood to the effect that the chest lead "does not in any way replace the routine electrocardiogram, but should be used as an adjunct to it" has a significant meaning. In this connection one is impelled to urge that in our present enthusiastic preoccupation with chest leads a parallel study of the standard leads should be persued with unabated diligence.

SUMMARY

The literature on chest leads in clinical electrocardiography is reviewed. This review is accompanied by comments on articles and case reports dealing with the subject.

The early literature appears to be colored by an unwarranted enthusiasm on the subject, leading on the one hand to an overemphasis of the value of chest leads, and on the other to a tendency to underrate the significance of abnormalities in the standard leads.

The conventional chest leads, Leads IV, V, and VI have been examined, and their significant features are discussed.

It is suggested that a chest lead for routine electrocardiography embody the following features: (a) that its tracing record maximal deflections and that it include well-defined auricular as well as ventricular complexes; (b) that its tracing be symmetrical with the standard leads; and (c) that the chest lead require but a single chest electrode.

The right arm chest lead has been found to fulfill these requirements.

Objections are offered to the numerical designation of chest leads. It is suggested that instead chest leads be designated by well-known anatomical landmarks, indicating the location of the principal or chest electrode.

Right pectoral (Rp), left pectoral (Lp), and apical (Ap) leads are suggested as routine chest leads in clinical electrocardiography. In these the right arm attachment used in the standard leads serves as the fixed secondary electrode, and the principal or chest electrode is attached to the left arm cable.

It is concluded that while chest leads have found a permanent place in clinical electrocardiography, standard leads are still to be regarded as the more dependable, and a parallel study of standard lead tracings, particularly with reference to minor deviations, should be persued with at least as much attention as the study of chest leads.

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The American Heart Journal

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Official Organ of the American Heart Association

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Retrospect and Prospect

The appearance of this issue marks the completion of the first ten years of the existence of THE AMERICAN HEART JOURNAL, and the occasion is welcomed as offering an opportunity for the JOURNAL to express to its contributors and subscribers its deep appreciation of their constant, friendly support and cooperation.

By a coincidence this tenth anniversary is to be marked, also, by certain developments in the policy of the JOURNAL by which its scope will be widened and its usefulness, it is believed, much increased.

The recent extraordinarily rapid growth of interest in the peripheral vascular disorders and their study has led to a recognition by the workers in that field of the need of some form of organization and of some central outlet for their contributions.

As the result of recent conferences between a representative group of workers in the field of peripheral vascular disease and the directors of The American Heart Association it has been decided to establish in The American Heart Association a standing committee, or special section, for the study of the peripheral circulation. It is expected that THE AMERICAN HEART JOURNAL will serve as the chief medium for the publications of this group.

The problem of providing space for the anticipated large increase in the volume of material offered to the JOURNAL as the result of this ar-

rangement has been met by the willingness of the publishers to increase the number of issues from six to twelve a year. Beginning, then, in January, 1936, THE AMERICAN HEART JOURNAL will appear monthly instead of bimonthly as heretofore, and the editorial staff will be increased by the addition of Dr. Edgar V. Allen, of Rochester, Minn., to the Advisory Editorial Board and of Dr. Irving S. Wright, of New York City, as Associate Editor.

The increase in the number of issues will require a slight increase in the annual subscription price (from $7.50 to $8.50), but this will be more than offset, it is believed, by the offering of a new "journal membership" which provides both annual membership in The American Heart Association and a year's subscription to the JOURNAL for ten dollars.

In order that the changes planned may begin with a new volume of the JOURNAL it has been decided to continue Volume 10 to include the October and December numbers. For that reason the index, which usually is placed in the August issue, will be held over and published with the December number.

Society Transactions

NEW YORK COMMITTEE ON CARDIAC CLINICS, 1935

THE annual scientific meeting of the New York Committee on Cardiac Clinics was held in New York City on April 23, 1935. The following are abstracts of papers presented or read by title:

Studies on Circulation Time and Intravenous Pressure. William Benenson, M.D., and Elmer A. Kleefield, M.D.

ABSTRACT

Measurements of intravenous pressure by direct manometry and of circulation time from antecubital vein to tongue by the saccharin method were determined on sixty-seven hospitalized patients with varied illnesses. Cases were tabulated in order of increasing circulation times (8.2 to 48 seconds), with other comparable data. The first thirty-four with times of from 8.2 to 16 seconds are noncardiac and cardiac patients without clinical evidence of insufficiency. Eighteen cases comprise the second group, with circulation times ranging from 17.4 to 24 seconds. These are predominantly patients with severe cardiac disease without congestive failure. The last fifteen cases have times of from 24 to 48 seconds. All are clinically listed as patients with congestive failure.

There was no close correlation between intravenous pressure and cardiac function except that high pressures are encountered in extremely decompensated cardiac patients. In certain cases of congestive hepatomegaly there is a rise of intravenous pressure with palmar pressure on the liver. Saccharin timing shows a close correlation to cardiac function, is of aid in the study of the progress of a heart case, is occasionally helpful in differential diagnosis, and is safe, inexpensive, not unpleasant, and easy to perform.

Studies on the Diuretic Effect of Mercupurin in Man. Arthur C. DeGraff, M.D., J. Ernest Nadler, M.D., and Robert C. Batterman, M.D.

ABSTRACT

Controlled clinical studies were made on the diuretic properties of mercupurin (novurit), a complex mercurial salt having chemically bound to it 3.5 per cent theophylline. Patients with marked congestive heart failure who did not lose weight on complete rest in bed were chosen. Some of these patients had not responded to adequate doses of digitalis. Mercupurin produced a definite diuresis in twenty-two cases. The diuretic effect was increased by the addition of ammonium chloride. In eight cases the action of mercupurin was compared with that of salyrgan. Six of these gave a greater diuresis with mercupurin, and two cases were equivocal. Both salyrgan and mercupurin were studied in three cases by having the patient void every half hour on the days the diuretic was given. The peak of the diuretic effect occurred between the fourth and fifth hour with both drugs, and in each case mercupurin produced the greater diuresis.

When the mercupurin salt free of theophylline was used, the diuresis was less. Evidence submitted indicates that theophylline increases the diuretic effect in

man and lessens the local toxic action of the mercurial salts in animals. Neither mercupurin nor salyrgan caused any increase in the number of red blood cells in the urine or gave any other evidence of toxic effect on kidney.

A New Method of Heart Sound Recording. M. D. Feltenstein, M.D., and Myron M. Schwarzschild.

ABSTRACT

A method is used for recording heart sounds so that the graph agrees with auscultation. This is accomplished by introducing distortion in the electrical system of the recorder in order to stress high frequencies in the same way as the average ear does. All audible sounds are recorded, and no inaudible vibrations are registered. The records are made simultaneously with the electrocardiogram. Because of the smooth base line, timing is accurate. The salient characteristics of normal sounds are: (1) the first sound begins on the down stroke of R and persists from 0.06 to 0.12 second with an average frequency range of 75 to 500 cycles; (2) the second sound begins on the down stroke of T and persists from 0.04 to 0.06 second with an average frequency range of 50 to 350 cycles.

Murmurs are differentiated only by duration and position in the cardiac cycle. Sounds occurring prior to the apex of R are diastolic. Systolic murmurs may be recognized if the apparent first sound lasts more than 0.12 seconds. Split sounds do not include a silent interval and have a total duration within normal limits.

Action Potentials Near the Dorsal Surface of the Human Heart. Frederick H. Howard, M.D.

ABSTRACT

Records have been made by means of an esophageal electrode. While the exact position of this electrode has not yet been determined, it appears to have been placed in positions near the line of junction of the right and left sides of the heart.

The electrocardiogram so recorded is distinctive. Auricular activation is indicated by a brief diphasic deflection (P′), first positive, then negative. There is no P-wave. P′ occurs about 0.03 second after the beginning of impulse formation in the sinus and about 0.12 second before ventricular activation. In two cases in which the P-R interval was prolonged (0.40 second and 0.30 second in standard leads), P′ occurred about 0.10 second after P, suggesting that in some cases of delayed conduction there is a delay between the sinus and the point in the auricle near which the electrode lies. The initial ventricular complex is diphasic, first negative, then positive. It resembles closely that obtained from the precordium near the apex, except for the important difference that the sense of the deflection is reversed.

The Differentiation of Pulmonary and Cardiac Disease: The Evaluation of the Rôle of Each. Arthur M. Master, M.D., Harry L. Jaffe, M.D., and Simon Dack, M.D.

ABSTRACT

Dyspnea, orthopnea, cyanosis, coughing, and signs of congestive heart failure may appear in both cardiac and pulmonary disease. In fifty patients, history, physical examination, fluoroscopy, electrocardiogram, vital capacity, blood velocity, venous pressure, and exercise tolerance tests were utilized. In cardiac disease, precordial pain is likely to be more prominent. Severe cough, particularly with expectoration, is found in lung disease. Cardiac irregularities, such as auricular fibrillation and heart-block, gallop rhythm, and hypertension, indicate cardiac

involvement. The venous pressure is high in right heart failure but normal or low in pulmonary conditions. The circulation time, both arm-to-tongue and arm-to-lung, is normal or shortened in pulmonary disease and delayed in heart failure either right or left. The roentgen ray film and fluoroscopic examination may give evidence of heart and aortic involvement, for example, an enlarged or valvular type of heart, left ventricular hypertrophy, or a dilated or tortuous aorta, etc. In lung disease one may find a small heart or evidence of emphysema. The electrocardiogram may show definite evidence of myocardial involvement. The vital capacity is reduced in both states as is also the quantitative measurement of exercise tolerance. The basal metabolic rate is increased in congestive heart failure and in the presence of dyspnea or cyanosis.

Observations of the Roentgenographic Appearance of the Esophagus in the Diagnosis of Disease of the Heart and Aorta. John B. Schwedel, M.D.

ABSTRACT

The use of a barium-filled esophagus in the diagnosis of heart disease has become widespread enough to warrant a few critical remarks as to its limitations. Enlargement of the left auricle displaces the barium-filled esophagus posteriorly and in the case of associated rotation of the heart, also slightly to the right. The esophagus crosses the arch near its junction with the descending aorta. It is attached here very frequently by dense adhesions so that elongation of the aortic arch associated with various cardiac conditions will displace the barium-filled esophagus posteriorly and to the left. These are seen best in the left anterior oblique (posterior displacement) position and postero-anterior (displacement to left) positions. The displacement due to aortic elongation may simulate that of an enlarged left auricle and must be differentiated from it by noting carefully the course of the esophagus in the postero-anterior view. Occasionally, elongation of the aorta is also associated with enlargement of the left auricle presenting a curve, not only to the left in the postero-anterior view, but also to the right in its lower portion. In certain congenital anomalies there is a deviation of the aorta to a central position or even to a dextro position so that the indentation of the aorta is absent or may appear on the right side of the esophagus.

The Effect of Irregular Rhythms of the Heart on the Minute Volume Output of Blood From the Heart in Human Beings. Harold J. Stewart, M.D., Norman F. Crane, M.D., John E. Deitrick, M.D., and William P. Thompson, M.D.

ABSTRACT

Since there are few reports in the literature concerning the behavior of the heart when subject to abnormal rhythms, the following studies were undertaken. Measurements of the cardiac output were made by the Grollman acetylene method, of cardiac size from 2-meter x-ray films, of the arm-to-tongue circulation time by the injection of decholin intravenously, and of the venous pressure by direct method. The observations were made with the patients in the basal metabolic state.

1. Two patients suffering from paroxysmal auricular tachycardia and three patients exhibiting paroxysmal auricular fibrillation showed a smaller cardiac output and larger heart size than after reversion to regular cardiac mechanism.

2. In seven patients subject to rapid auricular fibrillation and exhibiting dyspnea and cyanosis, the cardiac output was less, the heart size was larger, the circulation time was longer, and in two instances the venous pressure was higher than after the ventricular rate had been slowed by giving digitalis. Now, when reversion to the normal rhythm occurred, the heart still being under the influence

of digitalis, the heart size either became smaller or remained unchanged, and the cardiac output either became greater or remained unaltered.

3. In two patients subject to permanent complete heart-block, the cardiac output was less than the normal predicted output. In one instance the stroke volume was greater than normal, and in the other less than normal.

It appears that rapid heart rates, whether the ventricles are beating regularly or irregularly, as well as the slow rate of complete heart-block, may be accompanied by a diminished cardiac output. A heart subject to auricular fibrillation in which the ventricular rate is slowed by digitalis may be as effective as a pump as is that same heart after reversion to normal rhythm, the heart still being under the influence of digitalis.

The Treatment of Rheumatic Carditis by Fever. Katherine Dodge, M.D., and Lucy Porter Sutton, M.D.

ABSTRACT

Among the patients with chorea treated at Bellevue Hospital with induced fever, sixteen children had evidence of acute carditis at the time of treatment. In nine all signs of activity had subsided by the end of treatment. In the remaining seven, signs were gone from a week or ten days following the end of the treatment. Because it appeared that the hearts of these children were benefited by induced fever, we are investigating the effects of fever therapy on carditis without chorea. Radiant energy is being used to produce fever.

We have treated two children with subacute bacterial endocarditis with neither benefit nor harm; one child with extremely severe acute carditis accompanied by polyarthritis and chorea, who subsequently improved, but whether as a result of treatment we were unable to say; and five children with subacute carditis, in two of whom the activity of the infection was strikingly and promptly arrested. In the other three improvement followed more slowly. We believe that fever therapy in the treatment of the subacute forms of active carditis merits further investigation and that the presence of certain forms of organic heart disease is not a contraindication to the use of fever therapy in the treatment of other diseases.

Characteristic Variations in Certain Experimental Chest Leads (Multiplane Chest Leads) With Experimentally Produced Myocardial Lesions, Experimental Ventricular Extrasystoles and Bundle-Branch Block. Joseph Weinstein, M.D., and David I. Abramson, M.D.

ABSTRACT

The results obtained with the use of multiplane chest leads in experimentally produced ventricular lesions in the cat and dog are reviewed. The right and left arm lead wires of the electrocardiograph were connected in various combinations to long linear electrodes placed on the chest wall anteriorly and posteriorly, parallel to and beyond the cardiac borders. The lesions were produced on various surfaces of both ventricles by means of an electric cautery. A study of the records obtained in 25 experiments revealed that the standard leads showed RS-T segment alterations in only about 50 per cent of the cases and Lead IV, in 66 per cent. There were instances when both the standard leads and Lead IV remained normal, but in all the experiments two or more of the multiplane chest leads demonstrated the presence of a lesion. It was observed that the position of the posterior or indifferent electrode was important in the detection of experimental myocardial lesions. It was found that three of these chest leads showed characteristic changes which invariably localized the lesion to one or the other ventricle. Further studies demonstrated the value of these chest leads in localization of experimental ventricular extrasystoles and bundle-branch block.

Department of Reviews and Abstracts

Selected Abstracts

Boothby, Walter M., and Rynearson, Edward H.: Increase in Circulation Rate Produced by Exophthalmic Goiter. Arch. Int. Med. 55: 547, 1935.

The circulation rate is increased in exophthalmic goiter. On the average, the greater the intensity of the disease, as measured by the oxygen consumption, the greater is the increase in the circulation rate.

The increase in the circulation rate in patients with exophthalmic goiter who are not treated with iodine, according to the investigations of Liljestrand and Stenstrom, is much greater than that which occurs in normal persons as the result of an increase in oxygen consumption due to work.

The relative increase in the circulation rate for a given increase in oxygen consumption is definitely less in patients who are treated with iodine than in those who have not received iodine. However, even under these conditions the increase in the circulation rate was, on the average, both in these cases and in those of Fullerton and Harrop, slightly greater than that produced in normal persons by a degree of work that caused a similar increase in oxygen consumption.

These facts suggest the hypothesis that in exophthalmic goiter, especially when the patient is not treated with iodine, there is present in the system a peculiar circulatory stimulant that causes a greater increase of the circulation rate than occurs in a normal subject as the result of a corresponding increase in oxygen consumption due to work. In exophthalmic goiter either this peculiar circulatory stimulant is decreased in amount or its effectiveness is lessened by medication with iodine.

Gladstone, Sidney A.: Cardiac Output and Related Functions Under Basal and Postprandial Conditions. Arch. Int. Med. 55: 533, 1935.

The acetylene method was applied in a study of the effect of digestion on the cardiac output in forty-four determinations on twelve subjects, of whom five had normal cardiovascular systems and seven presented some structural or functional abnormality. A source of error in the method of analysis of gases as originally proposed is discussed; a corrective procedure was applied, resulting in a tendency to increase the results for the cardiac output by approximately 3 per cent. As compared with the fasting condition, the effect of digestion on the circulatory system, as observed from one to three hours after taking a mixed meal of moderate size, consists in a slight increase in the systolic pressure and usually a less marked fall in the diastolic pressure, resulting in an increase in the pulse pressure. The cardiac output in the normal subject increased by from 11 to 47 per cent above the value during fasting, with an average increase of 25 per cent. In the abnormal subjects the increments varied by from 2 to 47 per cent, the average increase being 17 per cent. Several atypical responses in the subjects with pathological conditions were noted.

Weiss, Soma, and Ellis, Laurence B.: Oxygen Utilization and Lactic Acid Production in the Extremities During Rest and Exercise. Arch. Int. Med. 55: 665, 1935.

The utilization of oxygen and the production of lactic acid in the upper and lower extremities were compared in normal subjects and in patients having heart disease with and without congestive failure.

The average oxygen utilization during rest was essentially the same in the arm and in the leg. In heart disease without congestive failure, the utilization of oxygen during rest was normal in magnitude, but with congestive failure there was a tendency toward an increased peripheral utilization. This is evidence that in congestive failure the blood flow through the extremities is frequently reduced. Edema of the leg was not found to be associated with a relatively or absolutely increased local blood flow.

In the standing posture, the oxygen utilization of the extremities increased both in subjects with normal and in those with diseased cardiovascular systems, as a result, in part at least, of decreased blood flow.

Immediately after exercise the oxygen utilization increased markedly, but it returned to the level during rest within ten minutes. In a patient with heart disease the oxygen content of the femoral venous blood immediately after exercise was as low as 1.1 volumes per cent.

The average resting level of the lactic acid in the extremities was between 12 and 14 mg. for all groups. Immediately after the patients ceased walking, the lactic acid content of the femoral venous blood draining the active muscle more than doubled; it then fell rapidly during the next ten minutes but did not reach the level observed during rest within twenty minutes. The lactic acid content of the venous blood of the inactive arm rose slightly immediately after the exercise, but in ten minutes was similar to that of the leg, as a result of the mixing effect of the circulation. With the increasing severity of circulatory failure, there was a tendency for the femoral lactic acid to rise to a higher level than normal immediately after exercise and to fall more slowly.

With the exception of one case of congenital intraventricular septal defect, the etiology of the heart disease played no rôle in the nature of the peripheral circulatory response.

Certain patients showed marked cardiac disability, i.e., orthopnea, dyspnea, and low vital capacity of the lungs, and yet they had normal venous pressure, no edema, or hepatic enlargement and normal oxygen utilization and lactic acid response. The disability in these patients cannot be explained on the basis of the behavior of the peripheral circulation. When disturbances in the lactic acid production and peripheral circulation occur, they are the result and not the cause of heart failure.

Wilson, May G., Wheeler, George W., and Leask, Marguerite M.: The Relation of Upper Respiratory Infections to Rheumatic Fever in Children. II. Antihemolysin Titres in Respiratory Infections and Their Significance in Rheumatic Fever in Children. J. Clin. Investigation 14: 333, 1935.

There is presented a correlation of the clinical course with the bacteriological and immunological observations in eighty rheumatic subjects observed over a period of twelve to eighteen months.

The antistreptolysin titer for rheumatic subjects during apparent health gave a basal average of 135 units with a range of 25 to 715 units. There was no significant difference in the range of antistreptolysin titer observed for subjects during apparent health and during respiratory and rheumatic infection. A com-

parison of the antistreptolysin titers of inactive rheumatic subjects during respiratory and "streptococcal" respiratory infections showed a higher average titer and greater rise in titer for subjects experiencing respiratory infection unassociated with hemolytic streptococci in the pharyngeal flora. Two-thirds of the subjects experiencing rheumatic activity unassociated with respiratory infections did not exhibit a rise in antistreptolysin titer.

The antistreptolysin titer of active rheumatic subjects experiencing respiratory and "streptococcal" respiratory infections was similar to that observed for inactive rheumatic subjects experiencing these infections.

Following respiratory infections the antistreptolysin curve was characterized by a steplike elevation within one to three weeks of the onset, rising to a peak and falling by lysis within one or two months on remaining plateaulike at intermediate levels for longer periods, showing successive peaks following repeated respiratory infections.

The rise of the level of antistreptolysin in the serum following respiratory infections seemed directly related to the extent of the local and constitutional symptoms irrespective of the presence of hemolytic streptococci in the pharyngeal flora.

The antistreptolysin curves observed in subjects who developed respiratory infection simultaneously with, or during, rheumatic activity were similar to those described in subjects experiencing respiratory infections alone and bore no relation to the clinical course of rheumatic activity.

These observations do not support the assumption that a rise in the antistreptolysin titer of the serum is conclusive evidence of streptococcal respiratory infection. A rise in the antistreptolysin titer is not a necessary accompaniment of rheumatic fever in children.

McIntosh, Rustin, and Wood, Charles L.: Rheumatic Infections Occurring in the First Three Years of Life. Am. J. Dis. Child. **49**: 835, 1935.

From the records of the Babies Hospital covering a period of about twenty-five years, a group of twenty-four cases has been selected in all of which the disease appears to have begun before the age of three years and in which the evidence warrants the diagnosis of rheumatic infection. Six cases in which autopsy was performed are briefly presented.

The incidence of rheumatic infection in subjects under three years of age is probably greater than is generally recognized. History, symptoms, physical signs, and laboratory data in these cases are variable, and the clinical picture is more often that of general infection than that of a specific disease entity.

The outstanding feature of rheumatic infection manifest during the first three years of life is cardiac damage. In this series 96 per cent of the children exhibited either clinically or pathologically rheumatic heart disease.

Wheeler, George W., Wilson, May G., and Leask, Marguerite M.: The Relation of Upper Respiratory Infections to Rheumatic Fever in Children. III. The Seasonal Bacterial Flora of the Throat in Rheumatic and Non-Rheumatic Children. J. Clin. Investigation **14**: 345, 1935.

The data presented are based on a twelve-month study of 4,867 throat cultures from 123 rheumatic children and 1,231 cultures from 109 nonrheumatic children.

In addition to the basic flora of the throat, which is relatively constant for each individual, transient invaders are frequently found and tend to show their maximum incidence at well-defined seasons of the year. The seasonal incidence of various organisms in the pharyngeal flora must be considered in evaluating their possible etiological significance.

A comparison of throat cultures from rheumatic and nonrheumatic children shows no significant difference in the frequency or time of appearance of hemolytic streptococci in the throat. There was no noteworthy difference in the incidence of hemolytic streptococci in the throat during apparent health, upper respiratory infection, or rheumatic activity.

These findings do not suggest any definite relationship between hemolytic streptococci in the throat and rheumatic fever.

McGinn, Sylvester, and White, Paul D.: Acute Cor Pulmonale Resulting From Pulmonary Embolism. J. A. M. A. **104:** 1473, 1935.

Case histories of nine patients with the acute cor pulmonale secondary to pulmonary embolism are presented, accompanied by electrocardiographic studies in seven.

The symptoms and signs of extensive pulmonary embolism are variable, but predominating at first are those of shock—namely, collapse, pallor, sweating, apprehension, and a fall in blood pressure—followed by reaction to the infraction itself—namely, fever and elevation of the pulse and respiratory rates. None of these cases showed acute chest pain in the absence of pleural involvement, but most of the patients complained of substernal oppression and suffocation. Respiratory distress was marked in all cases.

If the state of shock from extensive pulmonary embolism is not too great, or after it has largely cleared, there may be found signs indicative of the secondary effect of the pulmonary embolism on the heart itself: that is, the acute cor pulmonale (dilatation of the right chambers) attended by pulmonary artery dilatation. Auscultation in these cases frequently showed accentuation of the pulmonary second sound, gallop rhythm, heard best in and just below the pulmonary valve region, and in two cases a "pericardial" friction rub with maximal intensity in the region of the second, third, and fourth interspaces. Cyanosis and engorgement of the neck veins were common manifestations at some time during the attack. These changes remained for only a short period in some of the cases. Pleural friction rubs were heard frequently.

Electrocardiograms taken soon after the occurrence of the pulmonary embolism showed similar changes in five of these patients, and, in two others taken some time after the attack, they had some of the characteristics, although they were less definite. The changes that appear significant are the presence of a Q-wave and late inversion of the T-wave in Lead III, the rather low origin of the T-wave with a gradual staircase ascent of the ST interval in Lead II, a prominent S-wave and a slightly low origin of the T-wave in Lead I and an upright T-wave (with inverted P and QRS waves) in Lead IV. In none of the cases was left axis deviation present at the time of the acute episode, whereas the tracings of two patients showed definite right axis deviation.

Electrocardiograms of two patients taken after recovery showed a complete disappearance of the changes already mentioned, and in a third patient there was almost a complete disappearance of abnormalities in a record taken forty-eight hours after the attack and twenty-seven hours after the first electrocardiogram. All three of these cases showed a change in the axis deviation; one had a prolonged P-R interval and in one case in Lead IV, the T-wave was reverting to normal (inverted). Follow-up studies indicate that the electrocardiographic changes are temporary and may disappear within forty-eight hours after the attack of pulmonary embolism.

It is probable that the changes observed clinically and the electrocardiographic variations in cases showing the acute cor pulmonale consequent to pulmonary embolism are due in large part to dilatation and partial failure of the chambers of the right side of the heart.

Magee, H. Ross, and Smith, Harry L.: Auricular Fibrillation in Hyperthyroidism. Am. J. M. Sc. **189**: 683, 1935.

Subjected to the effects of hyperthyroidism, old patients are prone to have auricular fibrillation; young patients, to maintain normal cardiac rhythm. The increased incidence of auricular fibrillation among older patients with hyperthyroidism is only partially attributable to the frequent occurrence of coronary sclerosis and hypertension after the age of forty. Advanced age itself, although unaccompanied by these processes, determines an increased susceptibility of the heart to auricular fibrillation and adds to the likelihood of its becoming decompensated under the stress of hyperthyroidism.

Among 210 cases of auricular fibrillation associated with hyperthyroidism, cardiac enlargement occurred in 79, in 35 of which there was no evidence of hypertension or of preexisting cardiac disease. In the same group of cases of auricular fibrillation, cardiac decompensation was present in 62; in 29 of these, hyperthyroidism was the only cause found for the cardiac decompensation. In only 2 cases did cardiac enlargement or decompensation afflict patients under forty years of age.

Auricular fibrillation resulting from hyperthyroidism is more often transient or intermittent than prolonged or continuous, especially when not accompanied by serious myocardial injury. The arrhythmia often develops, for the first time, during the immediate postoperative period, in which case it ceases spontaneously within a few hours to a few days. Even when cardiac injury has occurred, the fibrillation of the auricles is frequently replaced by normal sinus rhythm when the heart has been relieved of the strain of hyperthyroidism.

Hyperfunctioning adenomatous goiter results in auricular fibrillation and other signs of myocardial insufficiency more often than does exophthalmic goiter. The longer duration of hyperthyroidism in adenomatous goiter is a less important factor in producing the higher incidence of myocardial injury in this disease. Advanced age seems a much more important factor than duration or intensity of symptoms in determining the incidence of auricular fibrillation and myocardial insufficiency of patients with hyperthyroidism.

LaPlace, L. B.: Observations on the Effect of an Arteriovenous Fistula on the Human Circulation. Am. J. M. Sc. **189**: 497, 1935.

A case of traumatic femoral arteriovenous fistula is reported together with observations made with the fistula open, during external compression of the fistula, and after successful surgical repair. Significant changes in the cardiovascular system are described.

The inconstant relationship between the characteristic rise of blood pressure and slowing of the pulse rate on occlusion of the fistula leads to the conclusion that the bradycardiac reaction is not due exclusively to blood pressure changes.

The basal minute volume of the heart was increased 24 per cent by the fistula, but even in the presence of the increased output there was evidence of a relatively diminished capillary blood flow.

In the standing posture compression of the fistula caused a conspicuous increase in translucency of the lung fields as seen fluoroscopically, indicating a marked decrease in the blood content of the lungs.

The area of the silhouette and the transverse diameter of the heart were reduced by 45 per cent following treatment. It is concluded that the cardiac enlargement was due, as Lewis and Drury suggest, to a relatively inadequate coronary blood flow.

It is suggested that the total ablation of the thyroid in cases of coronary insufficiency may be of direct benefit to cardiac function in a manner analogous to the effect of closure of an arteriovenous fistula.

Quirno, Norberto, and Cobo, Jorge Lavalle: Capillaroscopy in States of Acrocyanosis. Rev. argent. de cardiol. **1**: 470, 1935.

As the result of capillary studies in patients suffering from acrocyanosis, the following characteristics were established: cyanotic fundus; stretching; dilatation and tortuosity of the loops, particularly of the venous branch; dilatation of the veins of the subpapillar plexus; very slow blood current and dark blood. The direct action of cold and warm water tests on capillaries, as well as the vasoconstricting effect of pituitary extract and vasoparalyzing effect of histamine, were observed. Different theories are suggested to explain the etiology of this vasomotor syndrome. It is believed that the alteration is due to a low tonus of the capillary venous system. The constricting effect of pituitary extract on capillaries suggests its use in cases of acrocyanosis.

De Takáts, Géza: Peripheral Vascular Disease. Its Significance for General Practitioners and Specialists. J. A. M. A. **104**: 1463, 1935.

This brief survey of the principles of examination, diagnosis, and management of peripheral vascular disease should focus some attention on these common and other significant disorders of peripheral circulation. Most of such material is primarily in the hands of the general practitioner. Some of them will complicate or obscure the problems of other specialties. The more intensive study of these peripheral circulatory disturbances will lead to earlier and better therapeutic results.

There is a brief discussion of methods of examining the peripheral pulse, skin temperature, posture, changes of color, cutaneous histamine reaction, blood pressure measurements, reflex dilatation to heat, and certain other methods.

Cohen, Alfred E., and Lewis, William H.: Lobar Pneumonia and Digitalis. Am. J. M. Sc. **189**: 457, 1935.

An analysis of 1,456 cases of lobar pneumonia observed in the Hospital of the Rockefeller Institute has been undertaken. The patients were admitted over a period of twenty-one years, from 1911 to 1932. An effort was made to ascertain what influence the action of digitalis has on the course of this disease. Its action, in favorable cases, in which auricular fibrillation and auricular flutter occur, appears to be beneficial.

The outcome in lobar pneumonia depends on the severity of the disease, which in turn depends especially on the presence of bacteriemia, the number of pulmonary lobes involved, and the existence of complications.

It is not certain whether the action of digitalis precipitates the occurrence of auricular fibrillation. If it does so, the number of cases is small, especially in the earlier decades.

The proximity of death does not determine the onset of auricular fibrillation. Even when it was present, it ceased in ten of eighteen cases before death.

Heart-block did not occur during the febrile period of lobar pneumonia except in those patients to whom a sufficient amount of digitalis was given to bring it about.

Graybiel, Ashton, and White, Paul D.: Diseases of the Heart: A Review of Contributions Made During 1934. Arch. Int. Med. 55: 842, 1935.

This review is introduced with the following statements:

There has not been a major contribution to the knowledge of heart disease during 1934. Minor advances have been made, however, and some recent gains consolidated. This review does not include all that has been done; it suffices merely to indicate certain trends and to cite some of the more interesting publications. While a few of the reports seem more wonderful than probable, an especially critical attitude has been avoided because the newness of the work prevents conclusion.

Bohning, A., and Katz, L. N.: The Four-Lead Electrocardiogram in Coronary Sclerosis. Am. J. M. Sc. 189: 833, 1935.

A total of 508 electrocardiograms taken with a Lead IV have been analyzed and the data tabulated and summarized. Two hundred were from patients clinically diagnosed to have coronary sclerosis, 50 from patients suspected of having coronary sclerosis but without definite symptoms, 100 from patients with suspected cardiac disease, 25 from individuals with normal hearts, and 133 from patients known to have other types of organic heart disease.

It was found that patients with coronary sclerosis showed abnormalities in Lead IV more often than any of the control groups.

The abnormalities in Lead IV in the patients with coronary sclerosis were almost always associated with abnormal findings in the conventional three leads, but the deviations were usually more striking in Lead IV.

Patients with coronary sclerosis having clinical evidence of myocardial incompetence showed abnormalities in Lead IV more often than patients without such myocardial incompetence.

The four major types of abnormal Lead IV found in patients with coronary sclerosis are described. They are the positive QRS_4 type (the most common), the negative QRS_4 type, the positive and diphasic T_4 type, and the deeply negative T_4 type.

The value of Lead IV in determining the status of the coronary circulation was confirmed by postmortem examination in seven cases of coronary sclerosis.

Serial four-lead electrocardiograms were obtained in 56 of the 200 patients with coronary sclerosis covering a period of from four months to two years or more. Analysis of these records and, in addition, those obtained on patients with recent coronary occlusion and other conditions showed the value of serial electrocardiograms in evaluating the state of the coronary circulation. This is particularly important because of the paucity of precise clinical evidence in a large number of such patients.

If records obtained in patients suffering from acute infectious processes, those taken on moribund patients, and those taken on patients given large doses of digitalis are excluded, then one can determine from serial four-lead electrocardiograms whether the coronary insufficiency is: (1) an acute transitory coronary insufficiency, i.e., angina pectoris, nocturnal dyspnea, cardiac asthma, or its equivalent; (2) a subacute sclerotis with myocardial infarction; (3) a chronic nonprogressive coronary insufficiency; or (4) a chronic progressive coronary insufficiency. This functional classification should prove as useful in evaluating the clinical course of the patients as the anatomical and etiological classifications.

This study emphasizes the importance of taking serial four-lead electrocardiograms in all patients suspected of having coronary disease in estimating the degree of insufficiency of the coronary circulation and the rate of its progress.

Schwab, Edward H., and Herrmann, George: Alterations of the Electrocardiogram in Diseases of the Pericardium. Arch. Int. Med. **55**: 917, 1935.

Seven cases of pericardial disease of various types are presented with abstracts of the clinical histories, complete physical and pertinent laboratory data, and serial electrocardiographic studies.

A complete review of the available literature on the subject has been attempted.

The similarity of the deviations in the RS-T sector in cases of pericardial effusion to those occurring in cases of coronary thrombosis with infarction is reiterated.

Attention is directed to the previously unmentioned but significant inversions of the T-wave which follow the changes in the RS-T segment in cases of excess fluid in the pericardial sac following reabsorption, thus continuing the electrocardiographic analogy between pericardial effusion and cardiac infarction.

The occurrence of progressive changes in the T-wave in acute fibrinous pericarditis without an accompanying effusion and without preceding abnormalities in the RS-T segment is emphasized.

An evaluation of the electrocardiographic differences between pericardial disease and cardiac infarction is presented. The absence of the development of significant abnormalities of the Q-wave in pericardial pathological processes is stressed. No information of differential diagnostic value is apparently to be derived from the use of Lead IV.

Some theories as to the mechanisms operative in the production of the types of electrocardiographic changes encountered, based on the clinical and experimental studies, are brought forth. The changes in the RS-T sector are apparently the result of ischemia of the cardiac muscle, and the progressive and retrogressive changes in the T-wave seem to be associated with organization and repair of the process in the epicardium and subepicardial myocardium.

Tennant, Robert, and Wiggers, Carl J.: The Effect of Coronary Occlusion on Myocardial Contraction. Am. J. Physiol. **112**: 351, 1935.

An optical myograph suitable for recording localized contractions from a ventricular surface and a technic for its correct application are described.

Normal myograms recorded simultaneously with aortic or ventricular pressure curves, though slightly deformed by oscillations during the isometric contraction and relaxation phases, clearly show the natural shortening which occurs during ventricular ejection and the lengthening which follows isometric relaxation.

Occlusion of a main coronary branch is followed by an evoluting series of myographic changes which indicate progressive enfeeblement of contraction to the extent that approximately within a minute the area stretches during isometric contraction, remains stretched during systolic ejection, and shortens quickly during isometric relaxation; in short, the myogram is completely inverted. Similar changes in contraction of the right ventricle occur following ligation of the right coronary artery. These observations demonstrate convincingly the functional inadequacy of described collateral circulation in normal hearts.

Reestablishment of the normal blood supply is followed by a reversed series of myographic changes with restoration of normal vigorous contractions provided that the period of ischemia is not too long in duration.

Failure of shortening is due to enfeeblement or abrogation of contraction and not to failure of impulses to reach the areas involved or to excite them.

The oxygen requirements for maintaining efficient contractions in the normally working heart are high as evidenced by the failure to maintain efficient contractions when an area is being perfused with highly oxygenated Locke's solution.

The observations supply tangible proof for the correctness of Orias' hypothesis that coronary occlusion produces an early abbreviation of total ventricular systole

with little or no decline of systolic pressure through a progressive decrease in amplitude and duration of contraction in the ischemic area. The results suggest further that the tendency for development of hypodynamic ventricular beats following coronary occlusion may not necessarily be due to fatigue of the remaining contracting fibers, but can be explained by loss of pressure in expanding the regions in which contractions are enfeebled or absent.

Several clinical implications of the results are briefly discussed.

Brown, Morton G.: The Relationship of Coronary Arteriosclerosis to Auricular Fibrillation With Special Reference to the Term "Arteriosclerotic Heart Disease." New England J. Med. **212:** 963, 1935.

An analysis was made of all cases coming to postmortem examination at the Peter Bent Brigham Hospital in the years 1913 to 1933 that showed auricular fibrillation exclusive of those with known rheumatic valvular disease. Particular attention was paid to the relation between this irregularity and disease of the coronary arteries. There were 119 cases, 91 with permanent and 28 with transient auricular fibrillation.

Hypertension was an etiological factor in 79.3 per cent of the cases with permanent fibrillation and in 86.5 per cent of the cases with transient fibrillation. Significant disease of the coronary arteries, although fairly frequent among those with hypertension, was not common as the sole factor in the development of permanent auricular fibrillation. Angina pectoris and coronary thrombosis were comparatively rare in patients who had had auricular fibrillation. There was a group of nine cases classified as of undetermined etiology which had no significant coronary artery disease or known previous hypertension.

There were nine cases showing other forms of heart disease, such as pericarditis and unrecognized stenosis of one of the valves. Finally there were additional fifteen instances with auricular fibrillation with no disease of the heart, five of which had hyperthyroidism.

Males predominated over females in a proportion of 2 to 1, and the ages ranged from thirty-nine to eighty-nine years with the majority between the years fifty to seventy. The heart weight was greater in the males and in those with permanent fibrillation than in the females or in those with transient fibrillation. Although congestive failure was the most common cause of death, it is of interest that pulmonary infarction was quite frequent and renal insufficiency rare.

Evidence is presented that marked peripheral sclerosis of itself need be no indication that the coronary arteries are sclerosed nor that the efficiency of the heart is in any way altered. From this it is therefore suggested that the term "arteriosclerotic heart disease" should be given up entirely or clarified in its expression.

Maynard, E. P., Jr., Curran, J. A., Rosen, I. T., Williamson, C. G., and Lingg, Claire: Cardiovascular Syphilis: Early Diagnosis and Clinical Course of Aortitis in Three Hundred and Forty-Six Cases of Syphilis. Arch. Int. Med. **55:** 873, 1935.

Present investigation was planned in order to study the natural history of syphilitic infection in relation to its effect on the cardiovascular system. Three hundred and forty-six patients with syphilis were studied. One hundred and forty-five (41.9 per cent) showed positive evidence of cardiovascular syphilis.

There were fourteen adult patients with congenital syphilis. In none of these was evidence of syphilis of the heart or aorta found.

The date of occurrence of the primary lesion was known in about half of the patients (55 per cent). The average age at which infection occurred was twenty-

six years. In a quarter of the patients studied, the chancre appeared before the age of twenty-one years.

One-fourth came for examination within one year, and one-half within ten years, after the occurrence of the initial lesion.

Evidence of cardiovascular syphilis was found within ten years after the appearance of the chancre in one-fourth of the cases, although the average interval from infection to the discovery of heart disease was twenty years. Symptoms were somewhat slower in making their appearance. One-fourth of the patients complained of symptoms within fourteen years after the development of the primary lesion. The average interval before symptoms occurred was twenty years.

Evidence of cardiovascular syphilis was found within the first three years after the appearance of the chancre in 8 patients (14 per cent). One in the entire group complained of symptoms referable to the heart.

Of twenty-one persons who were not examined until four to nine years after primary infection, six (28.6 per cent) revealed the presence of cardiovascular syphilis. Two of these suffered from aortic insufficiency, and one, from aneurysm. Symptoms were present in three of the six.

Among thirty-seven persons who were not examined until ten to nineteen years after the primary lesion, twenty-one (56.8 per cent) exhibited evidence of cardiovascular syphilis. Symptoms appeared in 51.3 per cent of these. Heart failure occurred in two patients, in both of whom aneurysm or aortic insufficiency was present.

In a group first observed from twenty to twenty-nine years after infection, 77.8 per cent exhibited signs of syphilitic heart disease; 40 per cent presented either aortic insufficiency or aneurysm. Symptoms were present in 78 per cent.

Of seventeen persons who were first examined thirty or more years after infection, fifteen revealed the presence of cardiovascular syphilis, and seven either the presence of aortic insufficiency or of aneurysm. Three quarters of them complained of cardiac symptoms.

Heart failure occurred only in those patients in whom aortic insufficiency, aneurysm, or involvement of a coronary artery developed.

There were significant changes in the electrocardiograms within ten years after the appearance of the chancre in only 10.4 per cent. No changes were found that could be considered characteristic of the condition.

A case is reported of a patient whose condition was diagnosed as syphilitic disease of a coronary artery, who died within two years after the occurrence of the chancre. Postmortem examination confirmed the diagnosis.

From this study the following conclusions were drawn:

Syphilis of the aorta can be recognized much earlier now than it could be in the past. In order to discover its presence, it is necessary that every syphilitic patient be examined regularly by methods used in making a diagnosis of cardiovascular disease. These examinations should be repeated once in six months or once a year.

Roentgenograms and fluoroscopic examination provide the most reliable means of deciding whether abnormality of the aorta is present in early syphilis.

Heart failure occurs only in those patients in whom syphilitic involvement has passed beyond the stage of simple aortitis. In the patients studied, myocardial failure appeared only after the development of aortic insufficiency, aneurysm, or narrowing of the coronary arteries. Multiple gummas may be regarded as a cause of heart failure, but this condition was not encountered in this study. It is well known that these four manifestations are late lesions. Symptoms of heart failure usually prompt patients to seek relief in clinics for cardiac disease. Since these tend to occur late in cardiovascular syphilis and since no special routine effort has been made in the past to examine syphilitic patients for evidence of cardiovascular

disease, the discovery of aortitis has been delayed. It is probably not true that syphilitic aortitis is a late lesion occurring, on the average, twenty years after the occurrence of the chancre. The authors' opinion is that involvement of the aorta begins soon after the chancre has appeared and that in the past discovery of the presence of the disease has been delayed by the late development of symptoms referable to the heart and more especially by inadequate methods of examination.

Schwarz, Herman, and Leader, Sidney: Latent Cardiac Complications Following Sydenham's Chorea. Am. J. Dis. Child. **49**: 952, 1935.

Seventy-five cases of so-called "pure" chorea were observed for from one to twelve years for evidence of cardiac involvement. The term "pure" chorea was used for the cases of chorea in which no other manifestations of rheumatism were noted clinically.

The longer the period of observation after the first attack of chorea, the higher was the percentage of cardiac involvement found; it apparently reached 100 per cent after seven or eight years, although the number of cases studied is too small to permit a definite statement. The signs of cardiac involvement developed insidiously, without recognizable attacks of rheumatic fever and in some cases without further attacks of chorea. In this series aortic murmurs, pericarditis, and subcutaneous nodules were never encountered.

It seems probable that what is said of rheumatic fever may also be said of chorea: "The heart is always involved." This probable cardiac involvement is added evidence that Sydenham's chorea is of rheumatic origin.

Ferris, Eugene B., Jr., and Myers, Walter K.: Initial Attacks of Rheumatic Fever in Patients Over Sixty Years of Age. Arch. Int. Med. **55**: 809, 1935.

Six cases of patients over sixty years of age with first attacks of rheumatic fever are reported. In three cases the diagnosis was confirmed at autopsy.

The course of the disease is similar to that in younger persons, except that the manifestations in the joints are possibly less intense and more persistent.

In older patients with polyarthritis, rheumatic fever should be considered as a diagnostic possibility.

McIntosh, Rustin, and Wood, Charles L.: Rheumatic Infections Occurring in the First Three Years of Life. Am. J. Dis. Child. **49**: 835, 1935.

The authors have selected from the records of the Babies Hospital, covering a period of about twenty-five years, a group of twenty-four cases in all of which the disease appears to have begun before the age of three years and in which the evidence warrants the diagnosis of rheumatic infection. This series and others illustrate that rheumatic infection is rare, although not exceptional, before the age of three years. The incidence is probably greater than is generally recognized.

The history, symptoms, physical signs, and laboratory data in these cases are variable, and the clinical history is more often that of general infection than that of a specific disease entity. The outstanding feature of rheumatic infection manifest during the first three years of life is cardiac damage. In this series 96 per cent of the children exhibited, either clinically or pathologically, rheumatic heart disease. Six cases in which autopsy was performed are briefly presented.

King, Robert L.: Heart Disease in the Pacific Northwest. Northwest Med. **34**: 154, 1935.

Heart disease ranks first as a cause of death in the states of the Pacific Northwest; furthermore, there has been a progressive rise in the mortality rate from this

cause, paralleling that of the United States Registration Area. Morbidity statistics compiled from hospital records are not reliable.

An analysis of the records of 556 private patients suffering from organic heart disease was made to determine the relative incidence of the various etiological factors, as well as their associated abnormalities. From this study hypertension (49.4 per cent), arteriosclerosis (20.3 per cent), and rheumatic fever (20 per cent) were found to represent the etiological factors in 90 per cent of the cases. Other less frequent factors were syphilis, thyrotoxicosis, and congenital maldevelopments. Acute rheumatic fever was rare, and syphilis was not a common cause of heart disease, findings which correspond to similar groups of private patients. Subacute bacterial endocarditis occurred in 2 per cent of the patients.

Katz, Louis N., Mayne, Walter, and Weinstein, William: Cardiac Pain: Presence of Pain Fibers in the Nerve Plexus Surrounding the Coronary Vessels. Arch. Int. Med. **55**: 760, 1935.

The observation of earlier workers is confirmed that occlusion of the coronary vessels and the surrounding tissue in the unanesthetized dog gives rise to an effective response resembling an anginal attack. The response from this procedure is similar to that obtained on compressing a superficial somatic sensory nerve, save for the inability of the animal to locate the site of irritation.

The results show that this response is due not to the occlusion of the coronary artery, but to stimulation of afferent fibers located in the nerve plexus surrounding the vessels. The evidence for this is:

1. Occlusion of a carefully isolated strip of the coronary artery caused no response, but a definite response was obtained when the undissected coronary vessels above and below this point were compressed.

2. Destruction of the nerve plexus with phenol and alcohol abolished the response to compression, but the response was still positive when a region above the phenolized area was stimulated.

3. Complete preliminary occlusion of the carefully isolated coronary artery did not prevent a positive response to compression above or below this point.

4. Pericardial tamponade following bleeding from a ruptured coronary artery caused syncope but no "anginal" response.

5. Positive affective responses occur only when the region about the coronary vessels is compressed. The rest of the myocardium and epicardium is insensitive to stimulation by pressure.

It is concluded that ischemia of the myocardium is at most one of many mechanisms operating on the nerve endings and nerve fibers which may give rise to anginal attacks.

Goldsmith, Grace A., Brown, George E.: Pain in Thrombo-Angiitis Obliterans. Am. J. M. Sc. **189**: 819, 1935.

There are seven distinct recognizable types of pain in thromboangiitis obliterans. The two major factors involved in the production of pain are ischemia and inflammation. The types of pain observed in arteriosclerosis obliterans are similar to those in thromboangiitis obliterans, with the exception that pain resulting from phlebitis and arteritis is absent.

Intermittent claudication was the initial symptom in more than 90 per cent of the cases in this series. The recognition of the arterial basis of this symptom is of crucial importance, as avoidance of ulcers and gangrene and preservation of limbs depend largely on early appreciation of the circulatory impairment. The presence

or absence of pulsations in the peripheral arteries should be determined in any case in which pain in the extremities is a prominent feature.

All types of pain present in this disease are amenable to treatment with the exception of that attributable to severe degrees of ischemic neuritis.

The decrease in the incidence of amputation in cases of thromboangiitis obliterans has followed, to a large degree, the effective treatment of pain.

Brams, William A., Golden, J. S.: The Early Response of Venesection With Observations on So-Called Bloodless Venesection. Am. J. M. Sc. **189**: 813, 1935.

So-called "bloodless venesection" failed to reduce venous pressure or to modify pulse rate or arterial pressure in patients with cardiac failure. These results are in contrast to the changes observed in the same patients after bloodletting.

The effects of ordinary venesection were studied in fifteen patients with cardiac failure. Observations were made every five minutes for a period of one hour after venesection was completed.

It was exceptional for either the systolic or diastolic arterial pressure to show an appreciable fall after venesection or during the period of observation. The same results were observed in patients with arterial hypertension as in those with normal pressure.

The pulse rate remained unchanged in all experiments.

Venous pressure fell consistently after bloodletting, the maximum drop occurring immediately after completion of venesection. The fall began early in the course of venesection, becoming apparent after removal of the first 100 c.c. of blood and continuing to drop as more blood was withdrawn. A partial return toward the control level within a few minutes was observed in the majority of instances, but the level of venous pressure after an hour was usually lower than the control level.

The fall in venous pressure was especially marked in cases in which venous hypertension existed, and the actual drop also depended greatly on the quantity of blood removed. The greatest drop usually occurred in cases of venous hypertension in which from 600 to 800 c.c. of blood were removed, though it so happened that a level nearer to normal was reached in the cases with a smaller blood removal.

The practical significance of the fall in venous pressure after venesection, in relation to cardiac failure, is briefly discussed.

Morlock, Carl G., Horton, Bayard T.: Variations in Blood Pressure in Renal Tuberculosis. Am. J. M. Sc. **189**: 803, 1935.

As a result of the analysis of the systolic blood pressures of 346 patients who had proved renal tuberculosis, we cannot concur in the opinion generally expressed that an active tuberculous lesion, regardless of its situation, has an accompanying arterial tension lower than normal. In the series of cases analyzed it was found that the vast majority of patients (approximately 76 per cent) had normal blood pressures, 22 per cent had hypertension—that is, a systolic pressure of 140 mm. of mercury or more—and approximately 2 per cent had hypotension—that is, a systolic blood pressure less than 100 mm. of mercury. The number of patients in this series with hypertension or hypotension was not any greater than was found in a larger control series of normal individuals in the same age groups.